10/811,428

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 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  OCT 23   The Derwent World Patents Index suite of databases on STN
                   has been enhanced and reloaded
 NEWS  4  OCT 30   CHEMLIST enhanced with new search and display field
 NEWS  5  NOV 03   JAPIO enhanced with IPC 8 features and functionality
 NEWS  6  NOV 10   CA/CAplus F-Term thesaurus enhanced
 NEWS  7  NOV 10   STN Express with Discover! free maintenance release Version
                   8.01c now available
 NEWS  8  NOV 20   CAS Registry Number crossover limit increased to 300,000 in
                   additional databases
 NEWS  9  NOV 20   CA/CAplus to MARPAT accession number crossover limit increased
                   to 50,000
 NEWS 10  DEC 01   CAS REGISTRY updated with new ambiguity codes
 NEWS 11  DEC 11   CAS REGISTRY chemical nomenclature enhanced
 NEWS 12  DEC 14   WPIDS/WPINDEX/WPIX manual codes updated
 NEWS 13  DEC 14   GBFULL and FRFULL enhanced with IPC 8 features and
                   functionality
 NEWS 14  DEC 18   CA/CAplus pre-1967 chemical substance index entries enhanced
                   with preparation role
 NEWS 15  DEC 18   CA/CAplus patent kind codes updated
 NEWS 16  DEC 18   MARPAT to CA/CAplus accession number crossover limit increased
                   to 50,000
 NEWS 17  DEC 18   MEDLINE updated in preparation for 2007 reload
 NEWS 18  DEC 27   CA/CAplus enhanced with more pre-1907 records
 NEWS 19  JAN 08   CHEMLIST enhanced with New Zealand Inventory of Chemicals
 NEWS 20  JAN 16   CA/CAplus Company Name Thesaurus enhanced and reloaded
 NEWS 21  JAN 16   IPC version 2007.01 thesaurus available on STN
 NEWS 22  JAN 16   WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data

 NEWS EXPRESS  NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8
 NEWS X25      X.25 communication option no longer available

Enter NEWS followed by the item number or name to see news on that
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FILE 'HOME' ENTERED AT 13:44:54 ON 16 JAN 2007

=> file medline
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'MEDLINE' ENTERED AT 13:45:18 ON 16 JAN 2007

 FILE LAST UPDATED: 13 Jan 2007 (20070113/UP).  FILE COVERS 1950 TO DATE.

  All regular MEDLINE updates from November 15 to December 16 have been
  added to MEDLINE, along with 2007 Medical Subject Headings (MeSH(R))
  and 2007 tree numbers.

  The annual reload will be available in early 2007.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> s tgf or (transforming growth factor) or (tumor growth factor) or (tumour growth
factor)
        27123 TGF
          165 TGFS
        27149 TGF
                (TGF OR TGFS)
        54576 TRANSFORMING
       870740 GROWTH
         1668 GROWTHS
       871971 GROWTH
                (GROWTH OR GROWTHS)
       785431 FACTOR
      2033443 FACTORS
      2525955 FACTOR
                (FACTOR OR FACTORS)
        38625 TRANSFORMING GROWTH FACTOR
                (TRANSFORMING(W)GROWTH(W)FACTOR)
       685837 TUMOR
       286811 TUMORS
       811496 TUMOR
                (TUMOR OR TUMORS)
       870740 GROWTH
         1668 GROWTHS
       871971 GROWTH
                (GROWTH OR GROWTHS)
       785431 FACTOR
      2033443 FACTORS
      2525955 FACTOR
                (FACTOR OR FACTORS)
          204 TUMOR GROWTH FACTOR
                (TUMOR(W)GROWTH(W)FACTOR)
       104125 TUMOUR
        66966 TUMOURS
       137421 TUMOUR
                (TUMOUR OR TUMOURS)
       870740 GROWTH
         1668 GROWTHS
       871971 GROWTH
                (GROWTH OR GROWTHS)
       785431 FACTOR
      2033443 FACTORS
      2525955 FACTOR
                (FACTOR OR FACTORS)
           44 TUMOUR GROWTH FACTOR
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                (TUMOUR(W)GROWTH(W)FACTOR)
L1        42938 TGF OR (TRANSFORMING GROWTH FACTOR) OR (TUMOR GROWTH FACTOR) OR
                (TUMOUR GROWTH FACTOR)

=> s l1 2003/py
MISSING OPERATOR L1 2003/PY
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s 2003/py
L2       571718 2003/PY
                (20030000-20039999/PY)

=> s l1 and 2003/py
         571718 2003/PY
                (20030000-20039999/PY)
L3         3147 L1 AND 2003/PY

=> s l3 and review
         465739 REVIEW
          58364 REVIEWS
         510647 REVIEW
                (REVIEW OR REVIEWS)
L4           135 L3 AND REVIEW

=> s l4 and (clinical or therapeutic or treatment or diseases)
        1511428 CLINICAL
             48 CLINICALS
        1511455 CLINICAL
                (CLINICAL OR CLINICALS)
        1519332 THERAPEUTIC
          19248 THERAPEUTICS
        1532733 THERAPEUTIC
                (THERAPEUTIC OR THERAPEUTICS)
        1974712 TREATMENT
         138460 TREATMENTS
        2029975 TREATMENT
                (TREATMENT OR TREATMENTS)
        1687604 DISEASES
L5           77 L4 AND (CLINICAL OR THERAPEUTIC OR TREATMENT OR DISEASES)

=> d 1-77 ibib abs

L5   ANSWER 1 OF 77     MEDLINE on STN
ACCESSION NUMBER:   2004217511     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 15115954
TITLE:              Liver fibrosis and inflammation. A review.
AUTHOR:             Kershenobich Stalnikowitz David; Weissbrod Alan Bonder
CORPORATE SOURCE:   Instituto Nacional de Ciencias Medicas y Nutricion Salvador
                    Zubiran.. kesd@quetzal.innsz.mx
SOURCE:             Annals of hepatology : official journal of the Mexican
                    Association of Hepatology, (2003 Oct-Dec) Vol. 2,
                    No. 4, pp. 159-63.  Ref: 41
                    Journal code: 101155885. ISSN: 1665-2681.
PUB. COUNTRY:       Mexico
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    General Review; (REVIEW)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200407
ENTRY DATE:         Entered STN: 30 Apr 2004
                    Last Updated on STN: 2 Jul 2004
                    Entered Medline: 1 Jul 2004
AB   Hepatic fibrosis, is a wound healing process characterized by accumulation
     of extracellular matrix proteins (ECM) especially collagen types I and
     III, as well as an increase in other extracellular matrix constituents
     such as proteoglycans, fibronectin and laminin in response to liver
     injury.  Recruitment of leukocytes takes place after the insult and
     requires several adhesion molecules.  Monocytes and macrophages are
     involved in inflammatory actions by producing nitric oxide and
     inflammatory cytokines.  As a consequence of chronic tissue damage
     stellate cells (SC) as well as extracellular matrix producting cells,
     undergo a process of activation characterized by proliferation, motility,
     contractility, and synthesis of extracellular matrix.  Activation of SC is
     regulated by several soluble factors, including cytokines, chemokines,
     growth factors, and products of oxidative stress.  TGF - b and
     IL- 6 are the two main fibrogenic cytokines.  Potential regulatory factors
     of the activation of SC are important targets for future antifibrogenic
     treatments.

L5   ANSWER 2 OF 77     MEDLINE on STN
ACCESSION NUMBER:   2004062556     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 14763137
TITLE:              [HER-ErbB family of receptors and their ligands: mechanisms
                    of activation, signals and deregulation in cancer].
                    La famille des recepteurs HER-ErbB et ses ligands:
                    mecanismes d'activation, signalisations et deregulations
                    dans le cancer.
AUTHOR:             L'Allemain Gilles
CORPORATE SOURCE:   ISBDC (Institut de signalisation, biologie du developpement
                    et cancer), CNRS UMR 6543, 28, avenue Valrose, 06108 Nice..
                    lallemain@unice.fr
SOURCE:             Bulletin du cancer, (2003 Nov) Vol. 90 Spec No,
                    pp. S179-85.  Ref: 45
                    Journal code: 0072416. ISSN: 0007-4551.
PUB. COUNTRY:       France
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    General Review; (REVIEW)
LANGUAGE:           French
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200402
ENTRY DATE:         Entered STN: 7 Feb 2004
                    Last Updated on STN: 18 Feb 2004
                    Entered Medline: 17 Feb 2004
AB   The topic of this review is first to analyze in normal
     conditions the signal transduction pathways induced by members of the
     HER-ErbB receptor family and their ligands, and second, to decipher some
     deregulations occurring in various cancer types.  As a result, new
     therapeutic opportunities will be mentioned.

L5   ANSWER 3 OF 77     MEDLINE on STN
ACCESSION NUMBER:   2004043977     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 14745974
TITLE:              TGF-beta signaling in human skeletal and
                    patterning disorders.
AUTHOR:             Serra Rosa; Chang Chenbei
CORPORATE SOURCE:   Department of Cell Biology, University of Alabama,
                    Birmingham 35294-0005, USA.. rserra@cellbio.bhs.uab.edu
CONTRACT NUMBER:    R01 AR45605 (NIAMS)
                    R01 AR46982 (NIAMS)
                    R01 HD43345 (NICHD)
SOURCE:             Birth defects research. Part C, Embryo today : reviews,
                    (2003 Nov) Vol. 69, No. 4, pp. 333-51.  Ref: 195
                    Journal code: 101167665. ISSN: 1542-975X.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    General Review; (REVIEW)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200405
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ENTRY DATE: Entered STN: 28 Jan 2004
Last Updated on STN: 5 May 2004
Entered Medline: 4 May 2004

AB Members of the transforming growth factor beta (TGF-beta) family of multifunctional peptides are involved in almost every aspect of development. Model systems, ranging from genetically tractable invertebrates to genetically engineered mice, have been used to determine the mechanisms of TGF-beta signaling in normal development and in pathological situations. Furthermore, mutations in genes for the ligands, receptors, extracellular modulators, and intracellular signaling molecules have been associated with several human disorders. The most common are those associated with the development and maintenance of the skeletal system and axial patterning. This review focuses on the mechanisms of TGF-beta signaling with special emphasis on the molecules involved in human disorders of patterning and skeletal development.

L5 ANSWER 4 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2004017113 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14714591
TITLE: How to make a good oocyte: an update on in-vitro models to study follicle regulation.
AUTHOR: Thomas Fiona H; Walters Kirsty A; Telfer Evelyn E
CORPORATE SOURCE: Institute of Cell and Molecular Biology, The University of Edinburgh, The King's Buildings, Mayfield Road, Edinburgh EH9 3JR, UK.
SOURCE: Human reproduction update, (2003 Nov-Dec) Vol. 9, No. 6, pp. 541-55. Ref: 197
Journal code: 9507614. ISSN: 1355-4786.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 13 Jan 2004
Last Updated on STN: 28 Jul 2004
Entered Medline: 27 Jul 2004

AB The ability to develop the technology to mature oocytes from immature oocytes in vitro is the ambition of many IVF clinics. If this can be successfully achieved then these techniques would be available to women with fertility problems. This would aid women at risk of premature ovarian failure, and possibly result in women no longer requiring an expensive drug regime and monitoring programme, which they currently have to undergo. The idea of harvesting immature oocytes for growth in vitro is not a new one, but progress has been slow in developing and optimizing techniques for use on humans and domestic species. At present, there are many technical reasons for the lack of progress in these species, such as length of culture and difficulty of follicle isolation. However, the major problem is our lack of knowledge of how the oocyte acquires developmental competence during its growth within the follicle. To date, culture systems have been developed that can support the growth and development of immature oocytes. These systems are beneficial in improving our knowledge of how autocrine/paracrine factors are involved in regulating and controlling oocyte development. However, only when we have a more in-depth understanding of what is required during development to make a viable oocyte, will we perhaps be able to develop in-vitro culture systems for clinical application. This review will focus on how analysis of early follicular growth and development, using in-vitro culture systems, has advanced our knowledge of the factors and process involved in the regulation of oocyte and somatic cell development.

L5 ANSWER 5 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2004006631 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14703706
TITLE: Interaction between injured corneal epithelial cells and stromal cells.
AUTHOR: Nakamura Kunihiko
CORPORATE SOURCE: Department of Ophthalmology, Keio University School of Medicine, Tokyo, Japan.. up4k-nkmr@asahi-net.or.jp
SOURCE: Cornea, (2003 Oct) Vol. 22, No. 7 Suppl, pp. S35-47.
Journal code: 8216186. ISSN: 0277-3740.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article;. (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 6 Jan 2004
Last Updated on STN: 12 Feb 2004
Entered Medline: 11 Feb 2004

AB PURPOSE: To review the effects of injured corneal epithelial cells on myofibroblastic cell formation in corneal stroma after excimer laser surgery. METHODS: Denudation of epithelium alone, photorefractive keratectomy (PRK), laser in situ keratomileusis (LASIK), and LASIK with denudation of epithelium were performed in rabbit eyes. Postoperative anterior stromal haze was assessed using a standard scale. Immunohistochemical methods were used to detect alpha-smooth muscle actin (alpha-SMA), a marker of myofibroblastic cells, and type III collagen in subepithelial corneal tissue. Rabbit corneal fibroblasts were cultured on collagen gels with or without cocultured corneal epithelial cells, or with partially scraped epithelial cells, on a companion plate separated by a permeable membrane. Gel thickness was measured daily to evaluate fibroblast-induced gel contraction. The total number of fibroblasts per gel was determined. Myofibroblasts were counted using immunocytochemical identification with alpha-SMA. Transforming growth factor (TGF)-beta was assayed in media on days 3 and 6; these procedures were also carried out in the presence of anti-TGF -beta antibody. RESULTS: Three weeks after surgery, the presence of alpha-SMA-positive long-extended and spindle-shaped stromal cells as well as synthesis of type III collagen were observed in the subepithelial stromal layer, corresponding to corneal haze, in eyes that underwent PRK and LASIK with denudation of epithelium, but not in those that underwent denudation of epithelium alone or LASIK. Gel contraction, number of alpha-SMA-positive cells, and total cell number were significantly greater on gels with injured epithelial cells than on those without epithelial cells or with uninjured epithelial cells, as was TGF-beta concentration in media. Anti-TGF-beta antibody eliminated these differences. CONCLUSIONS: The intact corneal epithelium might play an important role in curbing differentiation of myofibroblasts in corneal wound healing. Injured epithelial cells stimulate fibroblast myodifferentiation through one or more soluble factors, including TGF-beta.

L5 ANSWER 6 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003607406 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14690153
TITLE: Carcinoid--a comprehensive review.
AUTHOR: Schnirer Isac I; Yao James C; Ajani Jaffer A
CORPORATE SOURCE: Department of Gastrointestinal Oncology and Digestive Diseases, The University of Texas M.D. Anderson Cancer Center, Houston, Texas 77005-4341, USA.
SOURCE: Acta oncologica (Stockholm, Sweden), (2003) Vol. 42, No. 7, pp. 672-92. Ref: 248
Journal code: 8709065. ISSN: 0284-186X.
PUB. COUNTRY: Norway
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 24 Dec 2003
Last Updated on STN: 8 Jan 2004
Entered Medline: 7 Jan 2004

AB Carcinoid tumors originate from the neuroendocrine cells throughout the body and are capable of producing various peptides. Their clinical course is often indolent but can also be aggressive and resistant to therapy. We examined all aspects of carcinoid tumors including the molecular biology oncogenesis, role of angiogenesis, recent advances in imaging, and therapy. The Medline and Cancerlit databases were searched using carcinoid as the keyword. English language manuscripts were reviewed and relevant references from a total of 7741 were found. All titles were screened and all the relevant manuscripts were analyzed; we found 307 references pertinent to the history, epidemiology, clinical behavior, pathology, pathophysiology, molecular biology, radiologic imaging, supportive care of carcinoid syndrome, and results of therapeutic clinical trials. Management of patients with carcinoid tumors requires an understanding of the disease process and a multimodality approach. Introduction of long-acting somatostatin analogues has resulted in significant advances in the palliative care of patients with carcinoid syndrome. However, advanced carcinoid tumor remains incurable. Existing therapies for advanced disease have low biologic activity, high toxicity, or both. Clearly, more research is necessary in the areas of molecular biology, targeted therapy, and development of new drugs Future advances in this field need to focus on clinical and biological predictors of outcome. Early works in the area of tumor biology such as the role of p53, bcl-2, bax, MEN1, FGF TGF PDGF and VEGF expression are of interest and need to be explored further.

L5 ANSWER 7 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003602050 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14683500
TITLE: Emerging role of endoglin (CD105) as a marker of angiogenesis with clinical potential in human malignancies.
AUTHOR: Fonsatti E; Sigalotti L; Arslan P; Altomonte M; Maio M
CORPORATE SOURCE: Department of Medical Oncology, Centro di Riferimento Oncologico, IRCCS, Aviano 33081, Italy.. efonsatti@cro.it
SOURCE: Current cancer drug targets, (2003 Dec) Vol. 3, No. 6, pp. 427-32. Ref: 82
Journal code: 101094211. ISSN: 1568-0096.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 20 Dec 2003
Last Updated on STN: 11 Feb 2004
Entered Medline: 10 Feb 2004

AB Angiogenesis is crucial for tumor development and progression, and antiangiogenetic therapy represents a promising approach for cancer treatment. Thus, the in-depth understanding of the molecular mechanism(s) regulating angiogenesis, together with the characterization of molecules expressed by endothelial cells and involved in distinct steps of the angiogenetic process, will greatly improve the design of new and more effective therapeutic strategies in human malignancies. Endoglin (CD105), a cell membrane glycoprotein predominantly expressed on cellular lineages within the vascular system, and over-expressed on proliferating endothelial cells, is involved in blood vessels development and represents a powerful marker of neovascularization. CD105 binds several factors of the Transforming Growth Factor (TGF)-beta superfamily, a pleiotropic cytokine that regulates different cellular functions including proliferation, differentiation and migration. In human malignancies of different histotype, CD105 is highly expressed on endothelial cells of both peri- and intra-tumoral blood vessels, while it is weakly expressed or absent on neoplastic cells. This unique tissue distribution strongly suggests for a prognostic, diagnostic and therapeutic potential of CD105 in neoplastic diseases. In this review we will summarize the structural and functional features of CD105, as well as its tissue distribution in normal and neoplastic tissues. Furthermore, the practical implications of CD105 in human malignancies will also be discussed.

L5 ANSWER 8 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003571815 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12832715
TITLE: Michael Mason prize essay 2003. Why do leucocytes accumulate within chronically inflamed joints?.
AUTHOR: Buckley C D
CORPORATE SOURCE: Department of Rheumatology, MRC Centre for Immune Regulation, University of Birmingham, UK.. c.d.buckley@bham.ac.uk
SOURCE: Rheumatology (Oxford, England), (2003 Dec) Vol. 42, No. 12, pp. 1433-44. Electronic Publication: 2003-06-27. Ref: 62
Journal code: 100883501. ISSN: 1462-0324.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 16 Dec 2003
Last Updated on STN: 24 Jan 2004
Entered Medline: 23 Jan 2004

AB Chronic inflammation is characterized by the accumulation of leucocytes within tissues. In rheumatoid arthritis the inflammatory infiltrate shares many architectural features with lymphoid tissue. For example, CD4 T cells and B cells accumulate in perivascular lymphoid structures within synovial tissue. CD8 T cells and neutrophils are found predominantly within synovial fluid. What drives these distinctive lymphoid microstructures and the relative contribution of lymphocytes and stromal cells such as fibroblasts to this process is the subject of this review. Cellular interactions between leucocytes and stromal cells such as macrophages and fibroblasts are important in generating tumour necrosis factor-alpha within the inflamed synovium. Therefore understanding how leucocytes accumulate within the inflamed synovium is likely to provide new therapeutic approaches to modify the inflammatory process. We have found that fibroblasts play a dominant role in defining the disordered synovial microenvironment in rheumatoid arthritis. Through their production of a variety of cytokines (interferon-beta, transforming growth factor -beta) and constitutive chemokines (stromal cell-derived factor-1, CXCL12) they directly alter the behaviour of lymphocytes that accumulate within chronically inflamed joints leading to their inappropriate survival and retention. We have extended these observations to another chronic persistent rheumatic disease, Sjogren's syndrome, and found that ectopic production of the constitutive B cell-attracting chemokine BCA-1 (CXCL13) is associated with lymphocyte accumulation and lymphoid tissue formation. These findings suggest that stromal cells such as fibroblasts play an important role in the switch from acute resolving to chronic persistent arthritis by allowing lymphocytes to accumulate in the wrong place at the wrong time.

L5 ANSWER 9 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003566685 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14643161

TITLE: Angiogenesis and bone repair.
AUTHOR: Carano Richard A D; Filvaroff Ellen H
CORPORATE SOURCE: Department of Physiology, Genentech, 1 DNA Way MS 42, South San Francisco, CA 94080, USA.
SOURCE: Drug discovery today, (2003 Nov 1) Vol. 8, No. 21, pp. 980-9. Ref: 152
Journal code: 9604391. ISSN: 1359-6446.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 16 Dec 2003
Last Updated on STN: 22 Jan 2004
Entered Medline: 21 Jan 2004

AB The intimate connection, both physical and biochemical, between blood vessels and bone cells has long been recognized. Genetic, biochemical, and pharmacological studies have identified and characterized factors involved in the conversation between endothelial cells (EC) and osteoblasts (OB) during both bone formation and repair. The long-awaited FDA approval of two growth factors, BMP-2 and OP-1, with angiogenic and osteogenic activity confirms the importance of these two processes in human skeletal healing. In this review, the role of osteogenic factors in the adaptive response and interactive function of OB and EC during the multi-step process of bone repair will be discussed.

L5 ANSWER 10 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003543176 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14623404
TITLE: Collagen sponges for bone regeneration with rhBMP-2.
AUTHOR: Geiger M; Li R H; Friess W
CORPORATE SOURCE: Drug Product Development, Wyeth BioPharma, One Burtt Road, Andover, MA 01810, USA.. mgeiger@wyeth.com
SOURCE: Advanced drug delivery reviews, (2003 Nov 28) Vol. 55, No. 12, pp. 1613-29. Ref: 108
Journal code: 8710523. ISSN: 0169-409X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200405
ENTRY DATE: Entered STN: 19 Nov 2003
Last Updated on STN: 20 May 2004
Entered Medline: 19 May 2004

AB In the US alone, approximately 500,000 patients annually undergo surgical procedures to treat bone fractures, alleviate severe back pain through spinal fusion procedures, or promote healing of non-unions. Many of these procedures involve the use of bone graft substitutes. An alternative to bone grafts are the bone morphogenetic proteins (BMPs), which have been shown to induce bone formation. For optimal effect, BMPs must be combined with an adequate matrix, which serves to prolong the residence time of the protein and, in some instances, as support for the invading osteoprogenitor cells. Several factors involved in the preparation of adequate matrices, specifically collagen sponges, were investigated in order to test the performance in a new role as an implant providing local delivery of an osteoinductive differentiation factor. Another focus of this review is the current system consisting of a combination of recombinant human BMP-2 (rhBMP-2) and an absorbable collagen sponge (ACS). The efficacy and safety of the combination has been clearly proven in both animal and human trials.

L5 ANSWER 11 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003533989 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14611717
TITLE: Platelet-rich plasma: a promising innovation in dentistry.
AUTHOR: Tozum Tolga Fikret; Demiralp Burak
CORPORATE SOURCE: Department of Periodontology, Faculty of Dentistry, Hacettepe University, Sihhiye-Ankara, Turkey.. ttozum@hacettepe.edu.tr
SOURCE: Journal (Canadian Dental Association), (2003 Nov) Vol. 69, No. 10, pp. 664. Ref: 96
Journal code: 7907605. E-ISSN: 1488-2159.
PUB. COUNTRY: Canada
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Dental Journals; Priority Journals
ENTRY MONTH: 200311
ENTRY DATE: Entered STN: 13 Nov 2003
Last Updated on STN: 19 Dec 2003
Entered Medline: 20 Nov 2003

AB The goal of periodontal therapy is to protect and maintain the patient's natural dentition for his or her lifetime. More specifically, after periodontal regenerative surgery, the aim is to achieve complete wound healing and regeneration of the periodontal unit. A recent innovation in dentistry is the preparation and use of platelet-rich plasma (PRP), a concentrated suspension of the growth factors found in platelets. These growth factors are involved in wound healing and are postulated as promoters of tissue regeneration. This clinical update outlines the specific effects of these growth factors, both in vitro and in vivo, on periodontal wound healing. The review focuses on current animal and human trials using PRP to promote tissue regeneration and alveolar bone repair. The article goes on to describe the clinical benefits of PRP and the step-by-step preparation of PRP in the dental office.

L5 ANSWER 12 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003532632 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14609717
TITLE: Immunosuppression and transplant vascular disease: benefits and adverse effects.
AUTHOR: Moien-Afshari Farzad; McManus Bruce M; Laher Ismail
CORPORATE SOURCE: Department of Pharmacology and Therapeutics, Faculty of Medicine, University of British Columbia, 2176 Health Sciences Mall, Vancouver, BC Canada V6T 1Z3.
SOURCE: Pharmacology & therapeutics, (2003 Nov) Vol. 100, No. 2, pp. 141-56. Ref: 192
Journal code: 7905840. ISSN: 0163-7258.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 13 Nov 2003
Last Updated on STN: 2 Apr 2004
Entered Medline: 1 Apr 2004

AB Cardiac allograft vasculopathy (CAV) occurs within 5 years of transplantation surgery and represents the main cause of death in long-term heart transplant survivors. The detailed pathogenesis of CAV is unknown, but there are strong indications that immunologic mechanisms, which are regulated by nonimmunologic factors, are the major cause of this phenomenon. Cyclosporine A (CsA) is a frequently used immunosuppressive agent in transplant medicine to prevent rejection. The mechanism of action of CsA involves initial binding to cyclophilin to form a complex that then inhibits calcineurin (CN), leading to reduced interleukin (IL)-2 production as part of the signal transduction pathway for the activation of B-lymphocytes and T-lymphocytes. Based on this proposed mechanism, it

was expected that CsA should be an effective strategy in attenuating the host immune response against transplanted allograft tissue; however, CsA has not changed the outcome of CAV. Several mechanisms have been suggested for the ineffectiveness of CsA in long-term prevention of CAV. For example, routine therapeutic doses of CsA may block CN incompletely (50%), whereas complete blockade requires doses that are not clinically tolerable. Another explanation is the possible activation of T-cell receptors directly (CN independent) by the immune response, which induces protein kinase C theta (PKCtheta) and leads to IL-2 production and immune rejection. Moreover, there may be a role for nonimmunologic mechanisms, such as complement, which cannot be controlled by CsA, or CsA may cause hypercholesterolemia or induce overexpression of transforming growth factor-beta (TGF -beta). This review also compares the effect of CsA with other immunosuppressants in allograft artery preservation and their clinical efficacy.

L5 ANSWER 13 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003510322 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14501439
TITLE: Allergic chronic inflammation of the ocular surface in vernal keratoconjunctivitis.
AUTHOR: Bonini Stefano; Lambiase Alessandro; Sgrulletta Roberto; Bonini Sergio
CORPORATE SOURCE: Interdisciplinary Center for Biomedical Research (CIR) Laboratory of Ophthalmology, University of Rome Campus Bio-Medico, and G.B. Bietti Eye Foundation, Italy.. sbonini@mclink.it
SOURCE: Current opinion in allergy and clinical immunology, (2003 Oct) Vol. 3, No. 5, pp. 381-7. Ref: 56 Journal code: 100936359. ISSN: 1528-4050.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 1 Nov 2003 Last Updated on STN: 19 Feb 2004 Entered Medline: 18 Feb 2004
AB PURPOSE OF REVIEW: The purpose of this review is to describe the new immunopathologic features of vernal keratoconjunctivitis: the involvement of cytokines, growth factors, cells, mediators and neurotransmitters, as well as the mechanism leading to tissue remodelling. RECENT FINDINGS: Vernal keratoconjunctivitis is an allergic eye disease affecting young boys living in a warm climate. It is characterized by conjunctival giant papillae, hyperemia and frequent involvement of the cornea. Approximately 50% of the patients with vernal keratoconjunctivitis do not have a family or medical history of atopic diseases, and do not show IgE sensitization, suggesting that this disease is not solely IgE mediated. Vernal keratoconjunctivitis is a Th2 lymphocyte driven disease with a Th2 cytokine derived pattern, increased levels of mRNA for IL-3, IL-4, IL-5 and IL-13. Th2 lymphocytes induce IgE hyperproduction, activation of mast cells, eosinophils, neutrophils and their toxic products. An overexpression of adhesion molecules, RANTES, eotaxin and metalloproteinases contribute to chronic inflammation. A role for substance P and nerve growth factor has been postulated, as well as for other growth factors (epidermal growth factor, fibroblast growth factor and transforming growth factor beta 1) that induce fibroblast growth and new collagen production. Recent studies have also pointed out the role of resident conjunctival cells, such as epithelial cells and fibroblasts, in the inflammatory and remodelling process of vernal keratoconjunctivitis. The pathogenesis of the condition is probably multifactorial, with the interaction of the immune, nervous and endocrine systems. SUMMARY: Vernal keratoconjunctivitis is a chronic inflammatory and potentially blinding disease. Understanding of the complex interactions and cross talk between cells, cytokines and other mediators is relevant for new therapeutic approaches.

L5 ANSWER 14 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003505268 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14582671
TITLE: The hair follicle and immune privilege.
AUTHOR: Paus Ralf; Ito Natsuho; Takigawa Masahiro; Ito Taisuke
CORPORATE SOURCE: Department of Dermatology, University Hospital, Hamburg-Eppendorf, University of Hamburg, Hamburg, Germany.. paus@uke.uni-hamburg.de
SOURCE: The journal of investigative dermatology. Symposium proceedings / the Society for Investigative Dermatology, Inc. [and] European Society for Dermatological Research, (2003 Oct) Vol. 8, No. 2, pp. 188-94. Ref: 60 Journal code: 9609059. ISSN: 1087-0024.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 30 Oct 2003 Last Updated on STN: 3 Jun 2004 Entered Medline: 2 Jun 2004
AB This essay reviews the available evidence that the proximal hair follicle epithelium generates and maintains an area of relative immune privilege during a defined segment of the hair cycle (i.e., during anagen). This immune privilege is chiefly characterized by a very low level of expression of MHC class Ia antigens and by the local production of potent immunosuppressive agents, such as alpha-MSH and TGF -beta1. We discuss the putative functions of immune privilige of the anagen hair bulb, favoring the view that immune privilege serves mainly to sequester anagen- and/or melanogenesis-associated autoantigens from immune recognition by autoreactive CD8+ T cells. On this basis, we develop how the "immune privilege collapse model" of alopecia areata pathogenesis was conceived. In our discussion of the clinical implications of immune privilege, we outline the currently available evidence in support of this still hypothetical scenario to explain the initiation, progression, and termination of alopecia areata lesions. We review the most recent evidence from our laboratory that alpha-MSH, IGF-1, and TGF-beta1 can downregulate IFN-gamma-induced ectopic MHC class I expression in human anagen hair bulbs in vitro. Finally, we suggest that hair follicle-derived alpha-MSH, IGF-gamma, and TGF-beta1 form part of a constitutively active "IP restoration machinery" of the anagen hair bulb, which we propose to be recruited whenever the hair follicle suffers immune injury. Finally, we sketch some particularly promising avenues for future investigation into the far too long ignored hair follicle immune privilege.

L5 ANSWER 15 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003502193 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14519757
TITLE: The role of the combination of IL-2 and TGF-beta or IL-10 in the generation and function of CD4+ CD25+ and CD8+ regulatory T cell subsets.
AUTHOR: Horwitz David A; Zheng Song Guo; Gray J Dixon
CORPORATE SOURCE: Division of Rheumatology and Immunology, Department of Medicine, Keck School of Medicine of the University of Southern California, Los Angeles 90033-1034, USA.. dhorwitz@hsc.usc.edu
CONTRACT NUMBER: AI 41768 (NIAID)
SOURCE: Journal of leukocyte biology, (2003 Oct) Vol. 74,

No. 4, pp. 471-8. Ref: 87
Journal code: 8405628. ISSN: 0741-5400.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200311
ENTRY DATE: Entered STN: 29 Oct 2003
Last Updated on STN: 19 Dec 2003
Entered Medline: 18 Nov 2003

AB Recently, considerable attention has been focused on thymus-derived CD4+ regulatory T cells that constitutively express CD25 and have a contact-dependent, cytokine-independent mechanism in vitro. However, peripheral CD4+ and CD8+ T cells can also be induced to become regulatory T cells. Here we review our studies using the combination of IL-2 and transforming growth factor beta (TGF-beta) to generate regulatory T cell subsets ex vivo, and the work of others using IL-10 to induce suppressive activity. Under certain conditions, the autocrine effects of TGF-beta and IL-10 induce peripheral T cells to produce immunosuppressive levels of each of these cytokines. This effect of TGF-beta is IL-2 dependent. Under other conditions IL-2 and TGF-beta can induce CD4+ cells to develop potent contact-dependent, cytokine-independent regulatory activity. At present, there is considerable confusion concerning the mechanism of action of CD4+ CD25+ cells because cytokine-producing regulatory T cells generated in the periphery can express CD25 and other markers displayed by naturally occurring, thymus-derived regulatory T cells. We, therefore, propose a nomenclature that identifies thymus-derived and peripheral regulatory cells, and that also differentiates T regulatory cells from T helper cells. Because T regulatory cells broadly control T helper cell reactivity, the mechanisms that control regulatory cell function are also reviewed. Finally, the potential use of regulatory T cells generated ex vivo as an adoptive immunotherapy for certain autoimmune diseases, to prevent organ graft rejection, or to prevent pathologic host responses to infectious agents is discussed.

L5 ANSWER 16 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003500669 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14579185
TITLE: [New Insights into the Etiological Pathogenesis of Peyronie's Disease].
Neue Aspekte zur Atiopathogenese der Induratio penis plastica.
AUTHOR: Hauck E W; Hauptmann A; Haag S M; Weidner W
CORPORATE SOURCE: Justus-Liebig-Universitat Giessen, Klinik und Poliklinik fur Urologie und Kinderurologie, Giessen.
SOURCE: Aktuelle Urologie, (2003 Oct) Vol. 34, No. 6, pp. 387-91. Ref: 71
Journal code: 0421406. ISSN: 0001-7868.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 28 Oct 2003
Last Updated on STN: 23 Apr 2004
Entered Medline: 22 Apr 2004

AB This paper reviews the current knowledge of the etiological pathogenesis of Peyronie's disease. De la Peyronie himself supposed a connection with venereal diseases. Herein, infectious, traumatic, autoimmune and genetic causes are discussed. An important hypothesis is that the recurrent microtraumatisation of the tunica albuginea during sexual intercourse leads to small lesions that activate processes of wound healing and development of fibrotic plaque. According to recent data, an association with the antigens of the HLA-system could be ruled out. Transforming growth factor beta (TGF-beta) seems to have an important impact due to its increased expression in the plaque. Furthermore it is possible to induce a condition similar to Peyronie's disease by intratunical injection of cytomodulin - a substance with TGF-beta-like activity - in an animal model. As in other fibrotic diseases, an imbalance between nitric oxide (NO) and reactive oxygen species (ROS) seems to be of importance. The most important new insights were gained from cell-culture models in which increased expression of basic fibroblast growth factor (bFGF), as well as a change in cell cycle regulation (p53) and cytogenetic instability were observed.

L5 ANSWER 17 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003493774 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14571096
TITLE: Factors enhancing intestinal adaptation after bowel compensation.
AUTHOR: Botsios D S; Vasiliadis K D
CORPORATE SOURCE: 4th Surgical Clinic, Aristotle University of Thessaloniki, Thessaloniki, Greece.. keva@med.auth.gr
SOURCE: Digestive diseases (Basel, Switzerland), (2003) Vol. 21, No. 3, pp. 228-36. Ref: 119
Journal code: 8701186. ISSN: 0257-2753.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 23 Oct 2003
Last Updated on STN: 20 Apr 2004
Entered Medline: 19 Apr 2004

AB Intestinal failure (IF) refers to the condition in which certain causes lead to derangements in nutrient absorption capacity. Gut adaptation occurs in response to IF and it is both morphologic and physiologic in nature and can be mediated by growth factors and nutrients. Our paper reviews certain trophic growth factors that have important interactions relevant for intestinal growth, function and adaptation. DATA SOURCE: The literature was reviewed (data from both animal and human studies) and certain trophic factors that modulate intestinal adaptation are summarized. The factors reviewed are: epidermal growth factor, insulin-like growth factor I and II, transforming growth factor alpha and beta, neurotensin, interleukin-11, glucagon-like peptide-2, keratinocyte growth factor, human growth hormone, short-chain fatty acids, and glutamine. CONCLUSIONS: Growth factors augment intestinal proliferation, diminish programmed apoptosis, and modulate the adaptive process. They also have the potential to improve nutrient absorption in some bowel disease. The enhancement of gut adaptation may allow patients to transition of parenteral/enteral to normal nutrition, in a shorter period of time, which reduce the rate of adverse effects caused by artificial nutrition and improve quality of life.

L5 ANSWER 18 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003491107 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14569209
TITLE: The role of chemokines in the pathogenesis of scleroderma.
AUTHOR: Atamas Sergei P; White Barbara
CORPORATE SOURCE: Baltimore Veterans Administration Medical Center, Department of Medicine, University of Maryland School of Medicine, Baltimore, Maryland 21201, USA.. satamas@umaryland.edu

CONTRACT NUMBER: 1R03AR47110 (NIAMS)
SOURCE: Current opinion in rheumatology, (2003 Nov) Vol. 15, No. 6, pp. 772-7. Ref: 53
Journal code: 9000851. ISSN: 1040-8711.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 22 Oct 2003
Last Updated on STN: 7 Feb 2004
Entered Medline: 6 Feb 2004

AB PURPOSE OF REVIEW: The triad of pathologic changes that defines systemic sclerosis (scleroderma) includes immune system activation with autoimmunity; an obliterative, proliferative small vessel vasculopathy; and fibrosis. Available data suggest that several cytokines, including chemokines, contribute to the development of scleroderma complications. This review focuses on chemokines and their contribution to tissue fibrosis and pulmonary hypertension in scleroderma. RECENT FINDINGS: Proteins and mRNAs for monocyte chemoattractant protein-1; pulmonary and activation-regulated chemokine; macrophage inflammatory protein-1, regulated upon activation normal T cell expressed and secreted; interleukin-8; and transforming growth factor -beta have been found in increased amounts in blood or involved tissue from scleroderma patients. These factors are likely to contribute directly to tissue damage in scleroderma through several pathways, including stimulation of extracellular matrix production, induction of TGF-beta production and activation, and chemoattraction of T cells and nonspecific inflammatory cells into tissues. SUMMARY: Multiple chemokines are part of the pathologic network that causes tissue damage in scleroderma, and, as such, may provide therapeutic targets in scleroderma.

L5 ANSWER 19 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003490604 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14568005
TITLE: Intervention strategies to prevent pathogenetic effects of glycated albumin.
AUTHOR: Cohen Margo P
CORPORATE SOURCE: Institute for Metabolic Research, University City Science Center, 3508 Market Street, Suite 420, Philadelphia, PA 19104, USA.. drmpcohen@aol.com
CONTRACT NUMBER: DK54143 (NIDDK)
DK54608 (NIDDK)
EY11825 (NEI)
SOURCE: Archives of biochemistry and biophysics, (2003 Nov 1) Vol. 419, No. 1, pp. 25-30. Ref: 84
Journal code: 0372430. ISSN: 0003-9861.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 22 Oct 2003
Last Updated on STN: 19 Dec 2003
Entered Medline: 11 Dec 2003

AB Modification of proteins by nonenzymatic glycation is one of the underlying factors contributory to the development of complications of diabetes. In general, the nature of this structural modification falls into two broad categories: nonenzymatic glycation per se, which refers to the attachment of free carbohydrate to proteins in the Amadori construct, and Advanced Glycation Endproducts (AGE), which refers to a heterogeneous group of carbohydrate-modified products generated from the Amadori adduct by oxidation, polymerization, and other spontaneous reactions. This review will focus on the role of nonenzymatically glycated proteins, and in particular glycated serum albumin, in the pathogenesis of diabetic complications, and on pharmacologic approaches to mitigate their deleterious effects. Potential intervention strategies to lessen the influence of AGE-modified proteins, as well as of other contributory abnormalities, are discussed elsewhere in this volume.

L5 ANSWER 20 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003472557 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14534681
TITLE: Carcinogenetic process in gallbladder mucosa with pancreaticobiliary maljunction (Review).
AUTHOR: Tsuchida Akihiko; Itoi Takao; Aoki Tatsuya; Koyanagi Yasuhisa
CORPORATE SOURCE: Department of Surgery, Tokyo Medical University, Tokyo 160-0023, Japan.. akibobo@hotmail.com
SOURCE: Oncology reports, (2003 Nov-Dec) Vol. 10, No. 6, pp. 1693-9. Ref: 51
Journal code: 9422756. ISSN: 1021-335X.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 10 Oct 2003
Last Updated on STN: 11 Jun 2004
Entered Medline: 10 Jun 2004

AB Pancreaticobiliary maljunction (PBM) is a congenital anomaly with a high incidence of biliary tract carcinoma. Pathological findings strongly suggest that there is a hyperplasia-dysplasia-carcinoma sequence in carcinogenesis of PBM. A molecular biological analysis revealed high incidence of cellular proliferation activating factors such as TGF -alpha, COX-2 from the hyperplasia stage. In addition, cellular proliferative activity including BrdU, AgNOR, PCNA, and Ki-67 was significantly higher in regular gallbladder mucosa without PBM. Furthermore, a high incidence of K-ras gene mutation could be seen in hyperplasia (13-63%) and microsatellite instability could be observed in 60% of all cases in dysplasia. In cancerous lesions, a high rate of overexpression of cyclin D1, beta-catenin, p53, as well as p53 gene mutation has been recognized. These results suggest that a multistep carcinogenetic process contributes to the carcinogenesis of PBM, similar to that of other cancers. In addition, after preventive operation with resection of the extrahepatic bile duct is performed, carcinogenesis in the remnant biliary tract or pancreatic duct is rarely found. Whether the carcinogenesis is a result of the accumulation of genetic alteration from shortly after birth, or a result of regurgitation of gastrointestinal juice due to hepaticoenterostomy, remains unknown. Since a high frequency of COX-2 is positive in PBM, COX-2 inhibitors such as NSAIDs may play an important role in preventing carcinogenesis.

L5 ANSWER 21 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003470386 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14532952
TITLE: The TGF-beta superfamily and its roles in the human ovary and placenta.
AUTHOR: Peng Chun
CORPORATE SOURCE: Department of Biology, York University, Toronto, ON, Canada.
SOURCE: Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC, (2003 Oct) Vol. 25, No. 10, pp. 834-44. Ref: 135
Journal code: 101126664. ISSN: 1701-2163.
PUB. COUNTRY: Canada

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 9 Oct 2003
Last Updated on STN: 27 Jan 2004
Entered Medline: 26 Jan 2004

AB The transforming growth factor-beta (TGF-beta) superfamily consists of a large group of growth and differentiation factors, such as TGF-betas, activins, inhibins, growth and differentiation factors (GDFs), and bone morphogenetic proteins (BMPs). These molecules act through specific receptor complexes that are composed of type I and type II serine/threonine receptor kinases. The receptor kinases subsequently activate Smad proteins, which then propagate the signals into the nucleus to regulate target gene expression. Several ligands in this family, such as TGF-betas, activins, inhibins, BMP-15, and GDF-9, play important roles in regulating human ovarian functions, including follicle development and maturation. Activin and TGF-beta are also involved in regulating placental development and functions. Abnormal expression or function of these ligands has been found in several pathological conditions. This review summarizes the role of the TGF-beta superfamily in human ovarian and placental regulation and function, and the potential clinical implications.

L5 ANSWER 22 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003447841 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14508854
TITLE: Translational research in lung cancer.
AUTHOR: Chen Yuhchyau; Okunieff Paul; Ahrendt Steven A
CORPORATE SOURCE: Department of Radiation Oncology, University of Rochester Medical Center, Rochester, New York 14642, USA.. yuhchyau@urmc.rochester.edu
SOURCE: Seminars in surgical oncology, (2003) Vol. 21, No. 3, pp. 205-19. Ref: 73
Journal code: 8503713. ISSN: 8756-0437.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 26 Sep 2003
Last Updated on STN: 11 Feb 2004
Entered Medline: 10 Feb 2004

AB Recent research advances in cancer and molecular biology have furthered our understanding of the etiology and natural history of lung cancer. Through translational research, a growing understanding of the molecular changes that underlie cancer progression has contributed to the development of novel molecular approaches for early detection, further defining prognosis, refining treatment schedules, identifying new therapeutic targets, and identifying patients at risk for treatment-related toxicity from aggressive therapy, such as pneumonitis and esophagitis. In this article, we review progress in molecular/gene screening and prognosis, and we present a clinical study, based on preclinical research, in which we apply low-dose radiosensitizing paclitaxel for locally advanced non-small-cell lung cancer (NSCLC); this resulted in superior local tumor control while keeping treatment toxicity low. We also review progress made in identifying cytokines: interleukin [IL]-1alpha, IL-6, and transforming growth factor [TGF] beta as markers for lung cancer treatment-related radiation pneumonitis. Finally, we summarize different targeted therapy approaches and discuss their application to clinical trials. Irrespective of the slow progress toward clinical improvements, we have gained much knowledge through translational research using new molecular and biologic technology. We believe that knowledge of lung cancer biology will continue to provide the foundation for future improvements in lung cancer treatment.

L5 ANSWER 23 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003444588 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14504780
TITLE: Angiogenesis factors in gliomas: a new key to tumour therapy?.
AUTHOR: Mentlein Rolf; Held-Feindt Janka
CORPORATE SOURCE: Anatomisches Institut, Universitat Kiel, Olshausenstrasse 40, 24098 Kiel, Germany.. rment@anat.uni-kiel.de
SOURCE: Die Naturwissenschaften, (2003 Sep) Vol. 90, No. 9, pp. 385-94. Electronic Publication: 2003-07-29. Ref: 89
Journal code: 0400767. ISSN: 0028-1042.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 24 Sep 2003
Last Updated on STN: 18 Dec 2003
Entered Medline: 4 Dec 2003

AB Angiogenesis, the formation of new blood vessels, is required for the growth and expansion of tumours. Gliomas, the most common brain tumours, are particularly highly vascularized and, therefore, serve as a model to elucidate the process of tumour angiogenesis and to investigate new anti-angiogenic therapies. This review describes the role of angiogenic factors in glioma angiogenesis and new strategies to inhibit glioma growth by application of anti-angiogenic substances. We focus on vascular endothelial growth factor (VEGF), but also examine the role of angiopoietin and pleiotropic factors such as platelet-derived growth factor (PDGF), pleiotrophin and transforming growth factor-beta (TGF-beta). Strategies to inhibit glioma growth by reducing the action of angiogenic factors, by the application of anti-angiogenic substances such as angiostatin or endostatin, or inactivation of endothelial cells, are discussed. These new anti-angiogenic therapies appear to have a high potential not only for the treatment of gliomas, but also of other tumours.

L5 ANSWER 24 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003440095 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14501440
TITLE: Fibrosis in ocular allergic inflammation: recent concepts in the pathogenesis of ocular allergy.
AUTHOR: Solomon Abraham; Puxeddu Ilaria; Levi-Schaffer Francesca
CORPORATE SOURCE: Department of Ophthalmology, Hadassah University Hospital, Jerusalem, Israel.
SOURCE: Current opinion in allergy and clinical immunology, (2003 Oct) Vol. 3, No. 5, pp. 389-93. Ref: 44
Journal code: 100936359. ISSN: 1528-4050.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 23 Sep 2003
Last Updated on STN: 19 Feb 2004
Entered Medline: 18 Feb 2004

AB PURPOSE OF REVIEW: Mast cells and eosinophils are the main

effector cells in allergic inflammation, but there is now compelling evidence that fibroblasts are also important players in the inflammatory response. In fact, they respond to different stimuli and release several mediators that modulate mast-cell and eosinophil functionality. In several allergic conditions such as vernal keratoconjunctivitis, asthma and atopic dermatitis the chronic presence of the inflammatory process has been associated with fibrosis and tissue remodeling, which in turn could cause irreversible alterations in the organ anatomy and functions. This review will discuss current advances in mast cell, eosinophil and fibroblast interactions in terms of their importance in the perpetuation of allergic inflammation and in contributing to the fibrosis and/or remodeling process in ocular allergy. As a main example of allergic ocular diseases associated with fibrosis, vernal keratoconjunctivitis is discussed in the light of recent findings. RECENT FINDINGS: Several studies have recently shown that fibroblasts can modulate the functions of mast cells and eosinophils through the membrane form of stem cell factor and granulocyte-macrophage colony-stimulating factor, respectively. On the other hand, fibroblasts can be affected by inflammatory mediators derived from mast cells and eosinophils, such as transforming growth factor beta and nerve growth factor and by the T helper type 2 cytokines, IL-4 and IL-13, and vernal keratoconjunctivitis-derived fibroblasts display altered functions. SUMMARY: Considerable useful information has been gained about the role of mast cells, eosinophils and fibroblasts in the perpetuation of allergic inflammation and tissue fibrosis and/or remodeling in general, and specifically in ocular allergy.

L5 ANSWER 25 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003427653 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12967780
TITLE: Immune regulation by regulatory T cells: implications for transplantation.
AUTHOR: Jonuleit Helmut; Adema Gosse; Schmitt Edgar
CORPORATE SOURCE: Department of Dermatology, University of Mainz, Hochhaus am Augustusplatz, Langenbeckstr. 1, 55101 Mainz, Germany.
SOURCE: Transplant immunology, (2003 Jul-Sep) Vol. 11, No. 3-4, pp. 267-76. Ref: 65
Journal code: 9309923. ISSN: 0966-3274.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 12 Sep 2003
Last Updated on STN: 27 Apr 2004
Entered Medline: 26 Apr 2004

AB The induction of antigen-specific T cell tolerance and its maintenance in the periphery are critical for the immune system to prevent autoaggressive immune responses. Our current state of knowledge about the immunoregulatory mechanisms responsible for T cell tolerance in the periphery offers new possibilities for immunomodulation to prevent transplant rejection as well as to diminish autoimmune reaction or chronic allergy. There is growing evidence that dendritic cells, besides their well-known T cell stimulatory functions, also maintain and regulate T cell tolerance in the periphery. This control function is exerted by certain maturation stages and subsets of dendritic cells, and can be further influenced and modulated by immunoregulatory cytokines and drugs. The regulatory functions of dendritic cells include the induction of T cell anergy, of T cells with regulatory properties and of T cells that produce immunosuppressive cytokines such as IL-10 or TGF-beta. Additionally, distinct subsets of resident regulatory T cells generated in the thymus play a central role in maintenance of peripheral tolerance by active suppression of effector T cell populations. These CD4(+)CD25(+) regulatory T cells inhibit a variety of autoimmune and inflammatory diseases and they are also efficient in the suppression of alloantigen responses. This review summarises the current knowledge regarding the immunoregulatory role of dendritic cells and the functional activities of resident regulatory T cells as guardians for peripheral T cell tolerance.

L5 ANSWER 26 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003415346 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12761669
TITLE: Do autologous growth factors enhance transforaminal lumbar interbody fusion?.
AUTHOR: Hee Hwan T; Majd Mohammad E; Holt Richard T; Myers Leann
CORPORATE SOURCE: Spine Surgery PSC, Louisville, Kentucky, USA.. hwantak@hotmail.com
SOURCE: European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society, (2003 Aug) Vol. 12, No. 4, pp. 400-7. Electronic Publication: 2003-05-22.
Journal code: 9301980. ISSN: 0940-6719.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 5 Sep 2003
Last Updated on STN: 22 Jan 2004
Entered Medline: 21 Jan 2004

AB Pseudarthrosis remains a significant problem in spinal fusion. The objective of our study was to investigate the effects of autologous growth factors (AGF) in instrumented transforaminal lumbar interbody spinal fusion (TLIF). A prospective review was carried out of 23 patients who underwent TLIF with application of AGF, with a minimum 2-year follow-up. Comparison with our historical cohort (without AGF application) was performed. Mean age at surgery was 44.3 years in the AGF treatment group. Twelve had a positive smoking history. Fourteen had undergone previous spinal surgeries. Thirteen received one-level fusions and ten received two-level fusions. The radiographic results showed a fusion rate of 100% in one-level fusions and 90% in two-level fusions. There was no significant difference in pseudarthrosis rates between the AGF treatment group and historical cohort. Excluding the cases with pseudarthrosis, there was faster bony healing in patients who had been treated with AGF application. This study indicates that although AGF may demonstrate faster fusions, it does not result in an overall increase in spinal fusion rates. Further studies are needed before AGF can routinely be used as an adjunct in spinal fusion.

L5 ANSWER 27 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003381119 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12916316
TITLE: Growth factor and regeneration of intervertebral disc.
AUTHOR: Wang Fei; Qu Dong-bin; Jin Da-di
CORPORATE SOURCE: Department of Spine Surgery, Nanfang Hospital, First Military University, Gungzhou, Guangdong, P. R. China 510515.
SOURCE: Zhongguo xiu fu chong jian wai ke za zhi = Zhongguo xiufu chongjian waike zazhi = Chinese journal of reparative and reconstructive surgery, (2003 Jan) Vol. 17, No. 1, pp. 73-5. Ref: 22
Journal code: 9425194. ISSN: 1002-1892.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 15 Aug 2003
Last Updated on STN: 18 Dec 2003
Entered Medline: 17 Dec 2003

AB OBJECTIVE: To review research progress of the relation between growth factor and repair of intervertebral disc. METHODS: The recent articles on growth factor and repair of intervertebral disc were extensively reviewed. The expression of growth factor in intervertebral disc and the effect of growth factor on disc cells were investigated. RESULTS: Some growth factors play roles in the development and degeneration of intervertebral disc. Exogenous growth factor can increase proliferation of disc cells and production of proteoglycans and collagens. Gene of growth factor can be transferred to intervertebral disc cell by adenovirus. CONCLUSION: Growth factor plays an important role in the regulation of development and degeneration of interertebral disc. The above results show that the feasibility of usage of growth factor in the treatment of disc degeneration and in repair and reconstruction of disc.

L5 ANSWER 28 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003373399 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12846694
TITLE: Camurati-Engelmann disease. Review of radioclinical features.
AUTHOR: Vanhoenacker F M; Janssens K; Van Hul W; Gershoni-Baruch R; Brik R; De Schepper A M
CORPORATE SOURCE: Department of Radiology, University Hospital Antwerp, Edegem, Belgium.. filip.vanhoenacker@planetinternet.be
SOURCE: Acta radiologica (Stockholm, Sweden : 1987), (2003 Jul) Vol. 44, No. 4, pp. 430-4.
Journal code: 8706123. ISSN: 0284-1851.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 12 Aug 2003
Last Updated on STN: 30 Aug 2003
Entered Medline: 29 Aug 2003

AB PURPOSE: To present a retrospective overview of the clinical and radiological features of Camurati-Engelmann disease (CED) in a large family with genetically proven CED. MATERIAL AND METHODS: Clinical features and imaging studies were available in 8 affected patients out of a large Jewish-Iraqi family with 21 affected members in four generations. The patients' ages ranged between 7 and 44 years. RESULTS AND CONCLUSIONS: The most frequent symptoms were pain and muscle weakness accompanied by waddling gait. Two patients were asymptomatic. Radiologically, the disease can be classified as a craniotubular hyperostosis. Typically, fusiform thickening of the diaphyseal portions of the long bones was seen in all 8 patients, but in 1 patient, metaphyseal involvement was observed as well. Radioclinical abnormalities were most often detected before the age of 30, and were usually more extensive at older age. Radiological abnormalities may precede the clinical signs. Concomitant broadening of the diaphyses of long bones and narrowing of the medullary canal suggest that both an excessive periosteal apposition of bone and a defective resorption of bone at the endosteal side of the long bones exist.

L5 ANSWER 29 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003369279 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12903835
TITLE: Molecular biologic aspects of cartilage and bone: potential clinical applications.
AUTHOR: Engstrand Thomas
CORPORATE SOURCE: Department of Surgical Sciences, Plastic Surgery, Uppsala University, Sweden.. thomas.engstrand@ortopedi.uu.se
SOURCE: Upsala journal of medical sciences, (2003) Vol. 108, No. 1, pp. 25-35. Ref: 35
Journal code: 0332203. ISSN: 0300-9734.
PUB. COUNTRY: Sweden
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 8 Aug 2003
Last Updated on STN: 30 Mar 2004
Entered Medline: 29 Mar 2004

AB The formation of cartilage and bone tissue from condensing mesenchymal stem cells is taking place in the early stage embryo, but also in the growth plate and during fracture repair in adults. Resident mesenchymal stem cells have been identified in bone marrow, periosteum, and in muscles. These pluripotent cells are attractive as therapeutic cells in cartilage and bone reconstructive procedures, since they can differentiate into chondrocytes and osteoblasts upon appropriate stimuli, such as certain growth factors. Members of the transforming growth factor-beta (TGF-beta) superfamily, including TGF-beta1-3, bone morphogenetic proteins (BMPs), and activins, are essential mediators in cell proliferation and differentiation and play regulatory roles in cartilage and bone formation. This review presents functional data on TGF-beta1 in cartilage formation, BMP2 and BMP3 in bone formation, and a role of the BMP-regulatory protein noggin in BMP2 processing. Potential clinical applications of these proteins are further demonstrated and discussed.

L5 ANSWER 30 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003364333 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12897477
TITLE: Bone morphogenetic proteins and spinal surgery.
AUTHOR: Sandhu Harvinder S
CORPORATE SOURCE: Department of Orthopaedic Surgery, Hospital for Special Surgery, Weill Cornell Medical College, New York, New York 10021, USA.. sandhuh@hss.edu
SOURCE: Spine, (2003 Aug 1) Vol. 28, No. 15 Suppl, pp. S64-73. Ref: 35
Journal code: 7610646. E-ISSN: 1528-1159.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 5 Aug 2003
Last Updated on STN: 21 Feb 2004
Entered Medline: 20 Feb 2004

AB STUDY DESIGN: A review of the literature concerning the use of recombinant human bone morphogenetic proteins 2 (rhBMP-2) and 7 (rhBMP-7) in spinal fusion. PURPOSE: To summarize the pertinent preclinical experiments that enabled regulated human clinical trials of recombinant bone morphogenetic proteins for spinal fusion and to update clinicians on the results of those trials. BACKGROUND: More than three decades of research involving thousands of scientists and academicians throughout the world have led to the clinical use of recombinant bone morphogenetic proteins for the treatment of spinal disease. METHODS: The published and presented scientific literature and the author's personal experience were examined. RESULTS AND CONCLUSIONS: Recent clinical data support the assertion that recombinant bone morphogenetic proteins can be used as complete bone graft substitutes in spinal fusion surgery. In some circumstances, the efficacy of these

factors for inducing successful fusion is superior to that of autogenous bone graft. RhBMP-2 is shown to be efficacious in several fusion applications, including intervertebral and lumbar posterolateral. Similar efficacy for rhBMP-7 has not yet been demonstrated, although relevant clinical studies are currently under way. The availability of these biologic agents will improve our ability to predictably treat spinal disease and may facilitate the further development of less invasive surgical innovations.

L5 ANSWER 31 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003361984 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12894871
TITLE: CSF-1 as a regulator of macrophage activation and immune responses.
AUTHOR: Sweet Matthew J; Hume David A
CORPORATE SOURCE: CRC for Chronic Inflammatory Diseases, Institute for Molecular Bioscience and Department of Microbiology/Parasitology, University of Queensland, Qld 4072, Australia.. m.sweet@imb.uq.edu.au
SOURCE: Archivum immunologiae et therapiae experimentalis, (2003) Vol. 51, No. 3, pp. 169-77. Ref: 102
Journal code: 0114365. ISSN: 0004-069X.
PUB. COUNTRY: Poland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 5 Aug 2003
Last Updated on STN: 25 Mar 2004
Entered Medline: 24 Mar 2004
AB Macrophage activation is a key determinant of susceptibility and pathology in a variety of inflammatory diseases. The extent of macrophage activation is tightly regulated by a number of pro-inflammatory cytokines (e.g. IFN-gamma, IL-2, GM-CSF, IL-3) and anti-inflammatory cytokines (e.g. IL-4, IL-10, TGF-beta). Macrophage colony-stimulating factor (CSF-1/M-CSF) is a key differentiation, growth and survival factor for monocytes/macrophages and osteoclasts. The role of this factor in regulating macrophage activation is often overlooked. This review will summarize our current understanding of the effects of CSF-1 on the activation state of mature macrophages and its role in regulating immune responses.

L5 ANSWER 32 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003355366 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12888715
TITLE: Surgical do's and don'ts of corneal dystrophies.
AUTHOR: Lee Eun Suk; Kim Eung Kweon
CORPORATE SOURCE: The Institute of Vision Research, Department of Ophthalmology, Yonsei University College of Medicine, Seoul, Korea.
SOURCE: Current opinion in ophthalmology, (2003 Aug) Vol. 14, No. 4, pp. 186-91. Ref: 55
Journal code: 9011108. ISSN: 1040-8738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200311
ENTRY DATE: Entered STN: 31 Jul 2003
Last Updated on STN: 4 Nov 2003
Entered Medline: 3 Nov 2003
AB PURPOSE OF REVIEW: Characteristics of corneal dystrophies have been described with regards to such as location in the cornea, morphology, material composition, and recurrence after penetrating keratoplasty. The main goal of this review is to describe the surgical methods in treating corneal dystrophies. RECENT FINDINGS: Laser in situ keratomileusis (LASIK) has been shown to aggravate corneal deposits in Avellino dystrophy exacerbation LASIK and hence should be avoided. Phototherapeutic keratectomy (PTK) has shown its usefulness in clearing opacities with visual improvement and prevents painful erosion, resulting in delay or postponement of corneal grafting in some corneal dystrophies. Mitomycin-C may be used topically in conjunction with PTK to reduce the recurrence of the opacities. Topical use of antibody to TGF -beta can also be considered to suppress recurrence of corneal opacities after PTK or lamellar keratectomy. SUMMARY: Clinicians must become more adept at choosing a treatment depending on different genotypes and future studies on treatment of corneal dystrophies should be focused on establishing treatment of categorized corneal dystrophies based on their chromosomal mutation.

L5 ANSWER 33 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003338911 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12871019
TITLE: Cartilage regeneration by gene therapy.
AUTHOR: Gelse K; von der Mark K; Schneider H
CORPORATE SOURCE: Nikolaus Fiebiger Center of Molecular Medicine, Dept. of Experimental Medicine I, University of Erlangen-Nuernberg, Germany.. hschneid@molmed.uni-erlangen.de
SOURCE: Current gene therapy, (2003 Aug) Vol. 3, No. 4, pp. 305-17. Ref: 130
Journal code: 101125446. ISSN: 1566-5232.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 22 Jul 2003
Last Updated on STN: 27 Mar 2004
Entered Medline: 26 Mar 2004
AB Damage of articular cartilage is a frequent clinical problem and is commonly considered to be irreversible. Full-thickness defects may lead to the formation of fibrous repair tissue of minor mechanical quality, while partial-thickness lesions hardly show any repair response. Surgical approaches often fail to restore the articular surface, facing the problem of incomplete chondrogenesis or rapid degradation of the repair tissue. However, advances in molecular biology have revealed the potential of growth factors, differentiation factors, and cytokines in directing cellular differentiation and metabolic activity. Anabolic factors including members of the TGF-beta superfamily, IGF-1, FGF, or HGF have proven their potential to stimulate chondrogenesis and synthesis of cartilage-specific matrix components, allowing the formation of a hyaline cartilage-like repair tissue in experimental studies. In addition, anti-catabolic or anti-inflammatory molecules, such as IL-4, IL-10, IL-1Ra, and TNFsR may also exert beneficial effects by inhibiting excessive cartilage degradation. Although it is questionable whether regeneration of hyaline cartilage implying a complete restoration of the articular surface by a tissue that is identical with the original can ever be achieved, all these molecules have been considered as suitable tools for cartilage repair. The transfer of the respective genes into the joint, possibly in combination with the supply of chondroprogenitor cells, might be an elegant method to achieve a sustained delivery of such therapeutic factors at the required location in vivo. This review focuses on the therapeutic molecules, the suitability of different viral and non-viral vectors for intraarticular gene transfer and the lessons learned from gene therapy studies on various animal models.

L5 ANSWER 34 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003336045 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12845620
TITLE: ECM homeostasis in renal diseases: a genomic approach.
AUTHOR: Eikmans M; Baelde J J; de Heer E; Bruijn J A
CORPORATE SOURCE: Department of Pathology, Leiden University Medical Center, Building 1, LI-Q, PO Box 9600, 2300 RC Leiden, The Netherlands.. M.Eikmans@LUMC.NL
SOURCE: The Journal of pathology, (2003 Jul) Vol. 200, No. 4, pp. 526-36. Ref: 141
Journal code: 0204634. ISSN: 0022-3417.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 19 Jul 2003
Last Updated on STN: 17 Sep 2003
Entered Medline: 16 Sep 2003

AB Chronic renal disease is in general histologically accompanied by a vast amount of scar tissue, ie glomerulosclerosis and interstitial fibrosis. Scarring results from excessive accumulation of extracellular matrix (ECM) components, a process driven by a plethora of cytokines and growth factors. Studies in experimental renal disease which target these regulators using gene therapy limit or prevent the development of scarring. This review focuses specifically on the role of transforming growth factor-beta, platelet-derived growth factor, connective tissue growth factor, hepatocyte growth factor, and epidermal growth factor. The results obtained in animal models hold promise for molecular intervention strategies in human renal disease. Microarray technology allows large-scale gene expression profiling in kidney tissue to identify common molecular pathways in a step towards discovery of new drug targets. Molecular techniques are expected to be used for diagnostic and prognostic purposes in nephrological practice to supplement renal biopsy. Several studies already show that molecular techniques might be of use in routine diagnostic practice. Improvement of diagnosis and prediction of outcome in renal patients might lead to more efficient and earlier therapeutic intervention.

L5 ANSWER 35 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003330843 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12860168
TITLE: Hematopoietic stem cell graft manipulation as a mechanism of immunotherapy.
AUTHOR: Talmadge James E
CORPORATE SOURCE: Nebraska Medical Center, University of Nebraska Medical Center 987660, Omaha, NE 68198-7660, USA.. jtalmadg@unmc.edu
SOURCE: International immunopharmacology, (2003 Aug) Vol. 3, No. 8, pp. 1121-43. Ref: 219
Journal code: 100965259. ISSN: 1567-5769.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 16 Jul 2003
Last Updated on STN: 30 Mar 2004
Entered Medline: 29 Mar 2004

AB Hematopoietic stem cell transplants (SCT) are used in the treatment of neoplastic diseases, in addition to congenital, autoimmune, and inflammatory disorders. Both autologous and allogeneic SCT are used, depending on donor availability and the type of disease being treated, resulting in different morbidity and outcomes. In both types of SCT, immune regulation via graft manipulation is being studied, although with highly different targeted outcomes. In general, autologous SCT have lower treatment-related morbidity and mortality, but a higher incidence of tumor relapse, and graft manipulation targets immune augmentation and/or the reduction of immune tolerance. In contrast, allogeneic SCT have a higher incidence of treatment -related morbidity and mortality and a significantly longer time of disease progression, and the targeted outcomes or graft manipulation focus on a reduction in graft versus host disease (GVHD). One source of the increased relapse rate and shorter overall survival (OS) following high dose chemotherapy (HDT) and autologous SCT is the immune tolerance that limits host response, both innate and antigen (Ag) specific, against the tumor. The immune tolerance that is observed is due in part to the tumor burden and prior cytotoxic therapy. Therefore, graft manipulation, as an adjuvant therapeutic approach in autologous SCT, is primarily focused on non-specific or specific immune augmentation using cytokines and vaccines. Recently, manipulation of the infused product as a form of cellular therapy has begun to also focus on approaches to reduce immune tolerance found in transplant patients, both prior to and following HDT and SCT. To this end, graft manipulation to reduce the presence of Fas Ligand (FasL)-expressing cells or interleukin (IL)10 and tumor growth factor (TGF)beta production has been proposed.In contrast to autologous transplantation, graft manipulation during allogeneic transplantation is used extensively. This includes limiting the infusion of T cells within the product or as a donor leukocyte infusion (DLI), resulting in a reduction in GVHD and the induction of long-term survivors. Indeed, allogeneic SCT provide the only curative therapy for patients with chronic myelogenous leukemia (CML), refractory acute leukemia, and myelodysplasia. The curative potential of allogeneic SCT is reduced, however, by the development of GVHD, a potentially lethal T-cell-mediated immune response targeting host tissues [Int. Arch. Allergy Immunol. 102 (1993) 309, J. Exp. Med. 183 (1996) 589]. The morbidity and mortality associated with GVHD limit this technology, resulting focus on those patients who have no alternative therapeutic options or who have advanced disease. Thus, allogeneic SCT provide one of the few statistically supported demonstrations of therapeutic efficacy by T cells (comparison of allogeneic to autologous transplantation). In contrast to autologous transplantation, control of GVHD following allogeneic SCT focuses on immune suppression and the induction of tolerance. Here too, graft manipulation is appropriate, and there are numerous studies of T-cell depletion to reduce GVHD, with or without the isolation and infusion of T cells as DLI. Additional strategies are examining the isolation and infusion of T cells with graft versus leukemia (GVL) activity to reduce GVHD and/or the infusion of genetically manipulated and/or selected cellular populations (monocytes or dendritic cells (DC)) to induce tolerance. Therefore, depending upon the type of transplant, the goals associated with graft manipulation can be radically different. In this review, we emphasize using graft manipulation to regulate immune tolerance and anergy in association with SCT. Although this paper focuses on hematopoietic SCT, it should be noted that these strategies are relevant to conditions other than neoplastic and congenital diseases, including solid organ transplants, and autoimmune and inflammatory diseases.

L5 ANSWER 36 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003318780 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12848344
TITLE: Basic and translational advances in cancer metastasis: Nm23.
AUTHOR: Ouatas Taoufik; Salerno Massimiliano; Palmieri Diane; Steeg

Patricia S
CORPORATE SOURCE: Women's Cancers Section, Laboratory of Pathology, Center for Cancer Research, National Cancer Institute, Bethesda, Maryland 20892, USA.. taoufik@mail.nih.gov
SOURCE: Journal of bioenergetics and biomembranes, (2003 Feb) Vol. 35, No. 1, pp. 73-9. Ref: 69
Journal code: 7701859. ISSN: 0145-479X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 10 Jul 2003
Last Updated on STN: 30 Mar 2004
Entered Medline: 29 Mar 2004

AB Cancer metastasis is a significant contributor to breast cancer patient morbidity and mortality. To develop new anti-metastatic therapies, we need to understand the biological and biochemical mechanisms of metastasis. Toward these efforts, we and others have studied metastasis suppressor genes, which halt metastasis in vivo without affecting primary tumor growth. The first metastasis suppressor gene confirmed was nm23, also known as NDP kinase. Using in vitro assays, nm23 overexpression resulted in reduced anchorage-independent colonization in response to TGF-beta, reduced invasion and motility in response to multiple factors, and increased differentiation. We hypothesize that the mechanism of action of Nm23 in metastasis suppression involves diminished signal transduction, downstream of a particular receptor. We hypothesize that a histidine protein kinase activity of Nm23 underlies its suppression of metastasis, and identify candidate substrates. This review also discusses therapeutic options on the basis of reexpression of metastasis suppressors.

L5 ANSWER 37 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003315786 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12845619
TITLE: The dynamic extracellular matrix: intervention strategies during heart failure and atherosclerosis.
AUTHOR: Heeneman Sylvia; Cleutjens Jack P; Faber Birgit C; Creemers Esther E; van Suylen Robert-Jan; Lutgens Esther; Cleutjens Kitty B; Daemen Mat J
CORPORATE SOURCE: Department of Pathology, Cardiovascular Research Institute Maastricht, University of Maastricht, 6200 MD Maastricht, The Netherlands.
SOURCE: The Journal of pathology, (2003 Jul) Vol. 200, No. 4, pp. 516-25. Ref: 109
Journal code: 0204634. ISSN: 0022-3417.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 8 Jul 2003
Last Updated on STN: 17 Sep 2003
Entered Medline: 16 Sep 2003

AB The extracellular matrix is no longer seen as the static embedding in which cells reside; it has been shown to be involved in cell proliferation, migration and cell-cell interactions. Turnover of the different extracellular matrix components is an active process with multiple levels of regulation. Collagen, a major extracellular matrix constituent of the myocardium and the arterial vascular wall, is synthesized by (myo)fibroblasts in the myocardium and smooth muscle cells in the medial arterial vascular wall. Its degradation is controlled by proteinases, which include matrix metalloproteinases. This review will focus on the impact of fibrosis and especially collagen turnover on the progression of heart failure and atherosclerosis, two of the main cardiovascular pathologies. We will discuss data from human studies and animal models, with an emphasis on the effects of interventions on collagen synthesis and degradation. We conclude that there is a dynamic (dis)balance in the rate of collagen synthesis and degradation during heart failure and atherosclerosis, which makes the outcome of interventions not always predictable. Alternative approaches for intervening in collagen metabolism will be discussed as possible therapeutic intervention strategies.

L5 ANSWER 38 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003311556 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12840703
TITLE: The T lymphocyte in food-allergy disorders.
AUTHOR: Eigenmann Philippe A; Frossard Christophe P
CORPORATE SOURCE: Department of Pediatrics, University Hospital of Geneva, Geneva, Switzerland.. Phillipe.Eigenmann@hcuge.ch
SOURCE: Current opinion in allergy and clinical immunology, (2003 Jun) Vol. 3, No. 3, pp. 199-203. Ref: 20
Journal code: 100936359. ISSN: 1528-4050.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 4 Jul 2003
Last Updated on STN: 10 Oct 2003
Entered Medline: 9 Oct 2003

AB PURPOSE OF REVIEW: While much attention is focused upon the role of IgE antibodies in food-allergy disorders, the T cell remains central to all forms, both IgE and non-IgE-mediated, of food-hypersensitivity responses. This review considers the central role of the T cell in this group of disorders and provides a comprehensive overview of recent studies that elucidate our understanding of the mechanisms involved in the pathogenesis of food allergy in regard to the role of the T cell. RECENT FINDINGS: Recent studies have defined a dynamic process involving T cell homing receptors (e.g. cutaneous lymphocyte antigen) and activation markers in food-hypersensitivity disorders. Modulation of the T-cell responses occurs through the recognition of dominant allergenic epitopes, the elaboration of regulatory cytokines (e.g. transforming growth factor-beta, IL-4, IL-5, tumor necrosis factor-alpha) and the influence of immunomodulatory microbial and environmental agents. The resulting disorders reflect T-cell dysregulation. SUMMARY: Significant recent advances in our understanding of the role of the T cell in food hypersensitivity have been made and will probably contribute to improved diagnostic and treatment methods in the near future.

L5 ANSWER 39 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003310730 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12839119
TITLE: Cow's milk allergy: a new understanding from immunology.
AUTHOR: Walker-Smith John
CORPORATE SOURCE: University Department of Paediatric Gastroenterology, Royal Free Campus, Royal Free and University College Medical School, University College, London, United Kingdom.. johnwalker_smith@hotmail.com
SOURCE: Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology, (2003 Jun) Vol. 90, No. 6 Suppl 3, pp. 81-3. Ref: 7
Journal code: 9503580. ISSN: 1081-1206.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 4 Jul 2003
Last Updated on STN: 22 Aug 2003
Entered Medline: 21 Aug 2003

AB BACKGROUND: Because of the high prevalence of cow's milk allergy as one of the most frequent clinical presentations of food allergy in infancy and early childhood, it is important to define the condition accurately. Allergy must be distinguished from the broader term food intolerance, which may be defined as a reproducible adverse reaction to the ingestion of a food or to any of its components, ie, proteins, carbohydrates, fats, and additives, and which includes toxic, metabolic, and allergic reactions. By contrast, food allergy may be defined as an adverse clinical reaction to a specific food component and that is immunologically mediated. The rapid increase in knowledge resulting from research in immunology in recent years has not only led to a better understanding of the basis for cow's milk allergy in infancy, but has also yielded considerable promise for improved diagnosis and management of the condition. OBJECTIVE: To review recent developments in immunology which demonstrate how they may lead to a better understanding of the clinical spectrum of cow's milk allergy in infants and children. DATA SOURCES: English language articles were selected from PubMed and selected abstracts that would have immediate, practical clinical implications. The review focuses on themes related to gastro-enterology, focusing upon the esophagus and small intestine. RESULTS: In cow's milk-sensitive esophagitis, there is dense infiltrate of eosinophils and increased T cell activation with upregulation of the chemokine eotaxin. In cow's milk-sensitive enteropathy, there is T cell activation, and it often results as a sequela of gastro-enteritis. Changing patterns in recent years suggests that sensitization occurs via mother's breastmilk to cow's milk and multiple food antigens. There is evidence of reduced Th1 response in these children. This is related to associated IgA deficiency and low levels of cytokine transforming growth factor beta.
CONCLUSIONS: The results of the present review demonstrate that the clinical manifestations of cow's milk allergy are very diverse, with differences between developing and developed countries. Understanding the immunologic mechanisms is of key importance in understanding this diversity.

L5 ANSWER 40 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003293451 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12820440
TITLE: The role of growth factors in central nervous system tumours.
AUTHOR: Nieder Carsten; Schlegel Juergen; Andratschke Nicolaus; Thamm Reinhard; Grosu Anca L; Molls Michael
CORPORATE SOURCE: Department of Radiation Oncology, Klinikum rechts der Isar, Technical University Munich, Ismaninger Str. 22, 81675 Munich, Germany.. nieder_radonc_tum@hotmail.com
SOURCE: Anticancer research, (2003 Mar-Apr) Vol. 23, No. 2C, pp. 1681-6. Ref: 63
Journal code: 8102988. ISSN: 0250-7005.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 25 Jun 2003
Last Updated on STN: 11 Jul 2003
Entered Medline: 10 Jul 2003

AB The role of growth factors in tumour growth and progression has increasingly been studied over the last few years. This review summarizes the available data and discusses their limitations as well as their potential influence on future therapeutic strategies. A large body of data suggests an important role of EGF, TGF-beta, PDGF and VEGF ligands and receptors in the vascularization of several brain tumour types, including gliomas and meningiomas. Recent experimental data indicate that inhibition of the signalling pathways may represent promising therapeutic strategies. Some inhibitory agents have now entered clinical trials, mainly for recurrent gliomas. Early results are presented.

L5 ANSWER 41 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003285340 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12812879
TITLE: A clinical, histopathological, and genetic study of Avellino corneal dystrophy in British families.
AUTHOR: El-Ashry M F; Abd El-Aziz M M; Larkin D F P; Clarke B; Cree I A; Hardcastle A J; Bhattacharya S S; Ebenezer N D
CORPORATE SOURCE: Department of Molecular Genetics, Institute of Ophthalmology, London EC1V 9EL, UK.. m_el_ashry@hotmail.com
SOURCE: The British journal of ophthalmology, (2003 Jul) Vol. 87, No. 7, pp. 839-42.
Journal code: 0421041. ISSN: 0007-1161.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 19 Jun 2003
Last Updated on STN: 13 Aug 2003
Entered Medline: 12 Aug 2003

AB AIMS: To establish a clinical, histopathological, and genetic diagnosis in two unrelated British families with Avellino corneal dystrophy (ACD). METHODS: Genomic DNA was extracted from peripheral blood leucocytes of all members participating in the study. Exons 4 and 12 of the human transforming growth factor beta induced (BIGH3) gene were amplified by polymerase chain reaction. The mutation and polymorphism were identified by direct sequencing and restriction digest analysis. A review of the patients' clinical symptoms and signs was undertaken and a histopathological study on corneal specimen obtained from the proband of one family after keratoplasty was performed. RESULTS: A heterozygous G to A transition at the second nucleotide position of codon 124 of BIGH3 gene was detected in all affected members of both families. This mutation changes an arginine residue to a histidine. The clinical diagnosis for ACD was more evident with advancing age. Histopathological study revealed granular deposits in the anterior stroma and occasional positive Congo red areas of amyloid deposition in the mid to deep stroma typical of ACD. CONCLUSIONS: This is the first report of ACD families in the United Kingdom and, furthermore, of BIGH3 gene mutation in British patients with this rare type of corneal dystrophy. The results indicate that BIGH3 gene screening along with clinical and histopathological examinations is essential for the diagnosis and clinical management of corneal dystrophies.

L5 ANSWER 42 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003280141 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12806875
TITLE: [Review on hypertrophic osteoarthropathy and digital clubbing].
Le point sur l'osteoarthropathie hypertrophique et l'hippocratisme digital.

AUTHOR: Vandemergel X; Decaux G
CORPORATE SOURCE: Service de Medecine Interne Generale, Hopital Erasme, U.L.B.
SOURCE: Revue medicale de Bruxelles, (2003 Apr) Vol. 24, No. 2, pp. 88-94. Ref: 56
Journal code: 8003474. ISSN: 0035-3639.
PUB. COUNTRY: Belgium
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 17 Jun 2003
Last Updated on STN: 26 Jul 2003
Entered Medline: 25 Jul 2003

AB Clubbing was first described by Hippocrates more than 2.500 years ago. It may be seen alone or as part of an entity called hypertrophic osteoarthropathy which include periostitis, arthritis and sometimes thickening and edema of the skin around the affected joints. Pulmonary diseases such as cancer, abscess, empyema, bronchiectasis and cystic fibrosis are the major diseases known to be associate with hypertrophic osteoarthropathy. Digestive tract cancer, cyanogenic congenital heart disease are well known association. Many theories have attempted to explain the appearance of this sign but few have persisted. In this article, we review characteristics, relation with etiology and the basis of the pathophysiology of hypertrophic osteoarthropathy and particularly of clubbing.

L5 ANSWER 43 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003272254 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12798347
TITLE: Regulation of osteogenic proteins by chondrocytes.
AUTHOR: Chubinskaya Susan; Kuettner Klaus E
CORPORATE SOURCE: Department of Biochemistry, Rush Medical College at Rush-Presbyterian-St. Luke's Medical Center, Chicago, IL 60612, USA.. Schubins@rush.edu
CONTRACT NUMBER: AR 47654 (NIAMS)
NIAMS 2-AP-39239 (NIADDK)
SOURCE: The international journal of biochemistry & cell biology, (2003 Sep) Vol. 35, No. 9, pp. 1323-40. Ref: 115
Journal code: 9508482. ISSN: 1357-2725.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 12 Jun 2003
Last Updated on STN: 9 Sep 2003
Entered Medline: 8 Sep 2003

AB The purpose of this review is to summarize the current scientific knowledge of bone morphogenetic proteins (BMPs) in adult articular cartilage. We specifically focus on adult cartilage, since one of the major potential applications of the members of the BMP family may be a repair of adult tissue after trauma and/or disease. After reviewing cartilage physiology and BMPs, we analyze the data on the role of recombinant BMPs as anabolic agents in tissue formation and restoration in different in vitro and in vivo models following with the endogenous expression of BMPs and factors that regulate their expression. We also discuss recent transgenic modifications of BMP genes and subsequent effect on cartilage matrix synthesis. We found that the most studied BMPs in adult articular cartilage are BMP-7 and BMP-2 as well as transforming growth factor-beta (TGF -beta). There are a number of contradicting reports for some of these growth factors, since different models, animals, doses, time points, culture conditions and devices were used. However, regardless of the experimental conditions, only BMP-7 or osteogenic protein-1 (OP-1) exhibits the most convincing effects. It is the only BMP studied thus far in adult cartilage that demonstrates strong anabolic activity in vitro and in vivo with and without serum. OP-1 stimulates the synthesis of the majority of cartilage extracellular matrix proteins in adult articular chondrocytes derived from different species and of different age. OP-1 counteracts the degenerative effect of numerous catabolic mediators; it is also expressed in adult human, bovine, rabbit and goat articular cartilage. This review reveals the importance of the exploration of the BMPs in the cartilage field and highlights their significance for clinical applications in the treatment of cartilage-related diseases.

L5 ANSWER 44 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003235452 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12757929
TITLE: Physiological and pathophysiological functions of the ecto-nucleotide pyrophosphatase/phosphodiesterase family.
AUTHOR: Goding James W; Grobben Bert; Slegers Herman
CORPORATE SOURCE: Department of Pathology and Immunology, Monash Medical School, Monash University, 3181, Victoria, Prahran, Australia.
SOURCE: Biochimica et biophysica acta, (2003 May 20) Vol. 1638, No. 1, pp. 1-19. Ref: 202
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 22 May 2003
Last Updated on STN: 13 Jul 2003
Entered Medline: 11 Jul 2003

AB The ecto-nucleotide pyrophosphatase/phosphodiesterase (E-NPP) multigene family contains five members. NPP1-3 are type II transmembrane metalloenzymes characterized by a similar modular structure composed of a short intracellular domain, a single transmembrane domain and an extracellular domain containing a conserved catalytic site. The short intracellular domain of NPP1 has a basolateral membrane-targeting signal while NPP3 is targeted to the apical surface of polarized cells. NPP4-5 detected by database searches have a predicted type I membrane orientation but have not yet been functionally characterized. E-NPPs have been detected in almost all tissues often confined to specific substructures or cell types. In some cell types, NPP1 expression is constitutive or can be induced by TGF-beta and glucocorticoids, but the signal transduction pathways that control expression are poorly documented. NPP1-3 have a broad substrate specificity which may reflect their role in a host of physiological and biochemical processes including bone mineralization, calcification of ligaments and joint capsules, modulation of purinergic receptor signalling, nucleotide recycling, and cell motility. Abnormal NPP expression is involved in pathological mineralization, crystal depositions in joints, invasion and metastasis of cancer cells, and type 2 diabetes. In this review we summarize the present knowledge on the structure and the physiological and biochemical functions of E-NPP and their contribution to the pathogenesis of diseases.

L5 ANSWER 45 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003225092 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12745005
TITLE: Antifibrotics and wound healing in glaucoma surgery.
AUTHOR: Lama Paul J; Fechtner Robert D
CORPORATE SOURCE: Glaucoma Division, New Jersey Medical School, Newark 07103,

USA.
SOURCE: Survey of ophthalmology, (2003 May-Jun) Vol. 48, No. 3, pp. 314-46. Ref: 129
Journal code: 0404551. ISSN: 0039-6257.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 15 May 2003
Last Updated on STN: 8 Jul 2003
Entered Medline: 7 Jul 2003

AB When medical and laser therapy fail to control intraocular pressure, glaucoma filtration surgery needs to be performed. Glaucoma surgery is unique in that its success is linked to interruption of the wound-healing response in order to maintain patency of the new filtration pathway. In this article we will review the wound-healing pathway and the pharmacologic interventions that have been employed clinically and experimentally to interrupt wound healing, particularly steroids and the antifibrotic agents 5-fluorouracil and mitomycin C. A review of the published literature looking at use of these agents to enhance success as well as the associated complications are presented, critiqued, and interpreted in order to put the studies in proper perspective. Future directions and recommendations regarding use of these agents are available and an introduction to newer wound modulating agents such as anti-transforming growth factor beta 2 is presented.

L5 ANSWER 46 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003218814 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12740224
TITLE: Combinatorial control of smooth muscle-specific gene expression.
AUTHOR: Kumar Meena S; Owens Gary K
CORPORATE SOURCE: Department of Molecular Physiology and Biological Physics, University of Virginia, 415 Lane Rd, MR5 Room 1220, PO Box 801394, Charlottesville, VA 22908, USA.. gko@virginia.edu
CONTRACT NUMBER: P01 HL19242 (NHLBI)
R01 HL38854 (NHLBI)
SOURCE: Arteriosclerosis, thrombosis, and vascular biology, (2003 May 1) Vol. 23, No. 5, pp. 737-47.
Electronic Publication: 2003-03-06. Ref: 123
Journal code: 9505803. E-ISSN: 1524-4636.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 13 May 2003
Last Updated on STN: 6 Mar 2004
Entered Medline: 5 Mar 2004

AB Alterations in the differentiated state of vascular smooth muscle cells (SMCs) are known to play a key role in vascular diseases, yet the mechanisms controlling SMC differentiation are still poorly understand. In this review, we discuss our present knowledge of control of SMC differentiation at the transcriptional level, pointing out some common themes, important paradigms, and unresolved issues in SMC-specific gene regulation. We focus primarily on the serum response factor-CArG box-dependent pathway, because it has been shown to play a critical role in regulation of multiple SMC marker genes. However, we also highlight several other important regulatory elements, such as a transforming growth factor beta control element, E-boxes, and MCAT motifs. We present evidence in support of the notion that SMC-specific gene regulation is not controlled by a few SMC-specific transcription factors but rather by complex combinatorial interactions between multiple general and tissue-specific proteins. Finally, we discuss the implications of chromatin remodeling on SMC differentiation.

L5 ANSWER 47 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003211406 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12732872
TITLE: Immunopathology and the gene therapy of lupus.
AUTHOR: Mageed R A; Prud'homme G J
CORPORATE SOURCE: Department of Immunology and Molecular Pathology, Royal Free and University College School of Medicine, London, UK.
CONTRACT NUMBER: AG15061 (NIA)
AR31203 (NIAMS)
AR39555 (NIAMS)
SOURCE: Gene therapy, (2003 May) Vol. 10, No. 10, pp. 861-74. Ref: 143
Journal code: 9421525. ISSN: 0969-7128.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 7 May 2003
Last Updated on STN: 24 Jun 2003
Entered Medline: 23 Jun 2003

AB Lupus is a chronic autoimmune inflammatory disease with complex clinical manifestations. In humans, lupus, also known as systemic lupus erythematosus (SLE), affects between 40 and 250 individuals, mostly females, in each 100 000 of the population. There are also a number of murine models of lupus widely used in studies of the genetics, immunopathology, and treatment of lupus. Human patients and murine models of lupus manifest a wide range of immunological abnormalities. The most pervasive of these are: (1) the ability to produce pathogenic autoantibodies; (2) lack of T- and B-lymphocyte regulation; and (3) defective clearance of autoantigens and immune complexes. This article briefly reviews immunological abnormalities and disease mechanisms characteristic of lupus autoimmunity and highlight recent studies on the use of gene therapy to target these abnormalities.

L5 ANSWER 48 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003202406 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12721353
TITLE: Stem cells as platforms for delivery of genes to enhance cartilage repair.
AUTHOR: Grande Daniel A; Mason James; Light Evan; Dines David
CORPORATE SOURCE: North Shore/Long Island Jewish Research Institute, Manhasset, NY 11030, USA.. dgrande@nshs.edu
SOURCE: The Journal of bone and joint surgery. American volume, (2003) Vol. 85-A Suppl 2, pp. 111-6.
Journal code: 0014030. ISSN: 0021-9355.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 1 May 2003
Last Updated on STN: 22 May 2003
Entered Medline: 21 May 2003

AB BACKGROUND: The long-held axiom put forth by Hunter in 1743, that cartilage once injured is incapable of healing, has been challenged by the technique of autologous chondrocyte transplantation. This conceptual

change in the way in which orthopaedists are approaching the problem of cartilage repair has spawned a myriad of new and innovative treatment modalities. This review will focus on the new techniques and directions that our facility and other investigators are exploring to restore functional articular cartilage. METHODS: To show the usefulness and effectiveness of local tissue-engineered gene therapy, we transduced periosteal stem cells known to have osteochondral potential with either bone morphogenetic protein-7 (BMP-7) or sonic hedgehog (Shh) gene. These cells were cultured to increase the number of cells and then were seeded onto bioresorbable polymer scaffolds. Full-thickness osteochondral defects were created in the mid-trochlear region of eighty New Zealand White rabbits, and the implants containing the transduced cells were placed in the defects. Animals were killed at six, eight, twelve, and twenty-six weeks postoperatively and were examined macroscopically and histologically. RESULTS: Periosteal-derived cambium-layer cells proliferated rapidly and were easily used for transfection of both the bone morphogenic protein-7 (BMP-7) and sonic hedgehog (Shh) genes. The control defects became filled with a mixture of fibrous and fibrocartilaginous tissue. The addition of either the BMP-7 or the Shh gene significantly enhanced the quality of the repair tissue, resulting in a much smoother surface and more hyaline-appearing cartilage. There was, however, a noticeable difference in the persistence of the cartilage phase between the group that received the Shh gene and the group that received the BMP-7 gene, with the subchondral compartment in the latter group seeming to remodel with bone much faster. CONCLUSION AND CLINICAL RELEVANCE: The results of these experiments clearly demonstrate the utility of tissue-engineering strategies in which gene therapy is used to locally influence the repair environment. It is interesting to note the relative differences in the two different gene responses with regard to skeletal development and the repair process. These differences could be related to the genes' temporal patterns in skeletal development.

L5 ANSWER 49 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003193035 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12711969
TITLE: Management of craniosynostosis.
AUTHOR: Panchal Jayesh; Uttchin Venus
CORPORATE SOURCE: Oklahoma University Health Science Center, Oklahoma 73104, USA.. Jayesh-Panchal@ouhsc.edu
SOURCE: Plastic and reconstructive surgery, (2003 May) Vol. 111, No. 6, pp. 2032-48; quiz 2049. Ref: 76
Journal code: 1306050. ISSN: 0032-1052.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 25 Apr 2003
Last Updated on STN: 23 May 2003
Entered Medline: 22 May 2003

AB Learning Objectives: After studying this article, the participant should be able to: 1. Review the etiopathogenesis of craniosynostosis and craniofacial anomalies. 2. Develop a basic understanding of the clinical manifestations and diagnosis of craniofacial anomalies. 3. Describe the surgical principles of managing craniosynostosis and craniofacial anomalies.Craniosynostosis, or the premature closure of calvarial sutures, results in deformed calvaria at birth. Although the etiology of craniosynostosis is currently unknown, animal experiments and a recent interest in molecular biology point toward interplay between the dura and the underlying brain. This interaction occurs by means of a local alteration in the expression of transforming growth factor, MSX2, fibroblast growth factor receptor, and TWIST. The fused suture restricts growth of the calvaria, thus leading to a characteristic deformation, each associated with a different type of craniosynostosis. Uncorrected craniosynostosis leads to a continuing progression of the deformity, and in some cases, an elevation of intracranial pressure. Clinical examination should include not only an examination of the skull but also a general examination to rule out the craniofacial syndromes that accompany craniosynostosis. Because deformational plagiocephaly, or plagiocephaly without synostosis, occurs secondary to sleeping in the supine position during the early perinatal period, the physician should be aware of this abnormality. Treatment for deformational plagiocephaly is conservative when compared with treatment for craniosynostosis, which requires surgery. Appropriate investigations should include genetic screening, radiologic examination with a computerized tomographic scan, and neurodevelopmental analysis. Surgical intervention should be performed during infancy, preferably in the first 6 months of postnatal life, to prevent the further progression of the deformity and possible complications associated with increased intracranial pressure. The principles of surgical intervention are not only to excise the fused suture but also to attempt to normalize the calvarial shape. Long-term follow-up is critical to determine the effect of the surgical outcome.

L5 ANSWER 50 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003180421 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12699349
TITLE: Endoglin (CD105): a target for anti-angiogenetic cancer therapy.
AUTHOR: Fonsatti E; Altomonte M; Arslan P; Maio M
CORPORATE SOURCE: Cancer Bioimmunotherapy Unit, Department of Medical Oncology, Centro di Riferimento Oncologico, IRCCS, Aviano 33081, Italy.. efonsatti@cro.it
SOURCE: Current drug targets, (2003 May) Vol. 4, No. 4, pp. 291-6. Ref: 76
Journal code: 100960531. ISSN: 1389-4501.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 18 Apr 2003
Last Updated on STN: 8 May 2003
Entered Medline: 7 May 2003

AB Targeting of tumor vasculature is a promising strategy for cancer treatment. Among endothelial cell markers, Endoglin, a cell membrane glycoprotein, is emerging as an attractive therapeutic target on angiogenetic blood vessels, and it currently represents a powerful marker to quantify tumor angiogenesis. In normal human tissues, Endoglin is weakly expressed on erytroid precursors, stromal cells and activated monocytes, whereas it is strongly expressed on proliferating endothelial cells. In human neoplasias of different histotype, Endoglin is mainly present on endothelial cells of both peri- and intra-tumoral blood vessels, while it is weakly expressed or absent on neoplastic cells. Endoglin is an accessory component of the receptor complex of Transforming Growth Factor (TGF)-beta, a pleiotropic cytokine that modulates angiogenesis by the regulation of different cellular functions including proliferation, differentiation and migration. Interestingly, the over-expression of Endoglin antagonizes several cellular responses to TGF-beta1, while its down-regulation potentiates cellular responses to TGF -beta1. In animal models, administration of radiolabeled anti-Endoglin monoclonal antibodies (mAb) efficiently images primary tumors, and naked or conjugated anti-Endoglin mAb suppress angiogenesis and tumor growth. In this review we will summarize the complex of experimental evidences pointing to Endoglin as a vascular target to design innovative bioimmunotherapeutic strategies in human neoplasias.

L5 ANSWER 51 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003179554 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12696985
TITLE: The roles of growth factors in tendon and ligament healing.
AUTHOR: Molloy Timothy; Wang Yao; Murrell George
CORPORATE SOURCE: Orthopaedic Research Institute, St George Hospital Campus, University of New South Wales, Sydney, Australia.
SOURCE: Sports medicine (Auckland, N.Z.), (2003) Vol. 33, No. 5, pp. 381-94. Ref: 59
Journal code: 8412297. ISSN: 0112-1642.
PUB. COUNTRY: New Zealand
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 17 Apr 2003
Last Updated on STN: 28 Sep 2003
Entered Medline: 26 Sep 2003

AB Tendon healing is a complex and highly-regulated process that is initiated, sustained and eventually terminated by a large number and variety of molecules. Growth factors represent one of the most important of the molecular families involved in healing, and a considerable number of studies have been undertaken in an effort to elucidate their many functions. This review covers some of the recent investigations into the roles of five growth factors whose activities have been best characterised during tendon healing: insulin-like growth factor-I (IGF-I), transforming growth factor beta (TGFbeta), vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), and basic fibroblast growth factor (bFGF). All five are markedly up-regulated following tendon injury and are active at multiple stages of the healing process. IGF-I has been shown to be highly expressed during the early inflammatory phase in a number of animal tendon healing models, and appears to aid in the proliferation and migration of fibroblasts and to subsequently increase collagen production. TGFbeta is also active during inflammation, and has a variety of effects including the regulation of cellular migration and proliferation, and fibronectin binding interactions. VEGF is produced at its highest levels only after the inflammatory phase, at which time it is a powerful stimulator of angiogenesis. PDGF is produced shortly after tendon damage and helps to stimulate the production of other growth factors, including IGF-I, and has roles in tissue remodelling.In vitro and in vivo studies have shown that bFGF is both a powerful stimulator of angiogenesis and a regulator of cellular migration and proliferation. This review also covers some of the most recent studies into the use of these molecules as therapeutic agents to increase the efficacy and efficiency of tendon and ligament healing. Studies into the effects of the exogenous application of TGFbeta, IGF-I, PDGF and bFGF into the wound site singly and in combination have shown promise, significantly decreasing a number of parameters used to define the functional deficit of a healing tendon. Application of IGF-I has been shown to increase in the Achilles Functional Index and the breaking energy of injured rat tendon. TGFbeta and PDGF have been shown separately to increase the breaking energy of healing tendon. Finally, application of bFGF has been shown to promote cellular proliferation and collagen synthesis in vivo.

L5 ANSWER 52 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003164209 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12682450
TITLE: Transforming growth factor -beta: a mediator of cell regulation in acute respiratory distress syndrome.
AUTHOR: Dhainaut Jean-Francois; Charpentier Julien; Chiche Jean-Daniel
CORPORATE SOURCE: Service de Reanimation Medicale, Pavillon Cornil, Faculte Cochin Port-Royal, Universite Paris 5, Hopital Cochin, Paris Cedex 14, France.
SOURCE: Critical care medicine, (2003 Apr) Vol. 31, No. 4 Suppl, pp. S258-64. Ref: 70
Journal code: 0355501. ISSN: 0090-3493.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 9 Apr 2003
Last Updated on STN: 30 Apr 2003
Entered Medline: 29 Apr 2003

AB OBJECTIVE: To review recent advances in the use of transforming growth factor (TGF)-beta in acute lung injury and to apply this knowledge to understanding the pathophysiology of this syndrome. DATA SOURCES AND STUDY SELECTION: Published research and review articles in the English language related to the role of TGF-beta in acute lung injury. DATA EXTRACTION AND SYNTHESIS: The cytokine TGF-beta plays a critical role in the resolution of tissue injury in multiple organs, including the lung. Following injury, TGF-beta has been most thoroughly evaluated during the late phases of tissue repair, where it plays a critical role in the development of pulmonary fibrosis. In contrast, recent animal studies showed that expression levels of several TGF -beta-inducible genes were dramatically increased as early as 2 days after the induction of injury. The integrin alpha(v)beta(6) activates latent TGF-beta in the lungs. Mice lacking this integrin were completely protected from pulmonary edema in a model of bleomycin-induced acute lung injury. Pharmacologic inhibition of TGF-beta also protected wild-type mice from pulmonary edema induced by bleomycin or Escherichia coli endotoxin. Similar findings also have been reported in patients in a clinical study evaluating TGF-beta in the bronchoalveolar lavage fluid during the course of acute respiratory distress syndrome (ARDS). Indeed, the bronchoalveolar lavage concentrations were dramatically increased as early as 1 day after the initiation of ARDS criteria and were correlated with decreases in the Pao(2)/Fio(2) ratio, suggesting an important role for TGF-b1 in the development of ARDS in humans. CONCLUSIONS: These studies suggest that TGF-beta not only participates in the late phase of acute lung injury, but also might be active early in acute lung injury and potentially could contribute to the development of pulmonary edema. Integrin-mediated local activation of TGF-beta is critical to the development of pulmonary edema in ARDS, and blocking TGF -beta or its activation could be an effective treatment for this disorder.

L5 ANSWER 53 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003151899 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12668602
TITLE: Vascular morphogenesis: tales of two syndromes.
AUTHOR: Marchuk Douglas A; Srinivasan Sudha; Squire Teresa L; Zawistowski Jon S
CORPORATE SOURCE: Department of Molecular Genetics and Microbiology, Duke University Medical Center, Box 3175, Durham, NC 27710, USA.. march004@mc.duke.edu
CONTRACT NUMBER: HL-49171 (NHLBI)
NS-43543 (NINDS)
SOURCE: Human molecular genetics, (2003 Apr 1) Vol. 12 Spec No 1, pp. R97-112. Ref: 187
Journal code: 9208958. ISSN: 0964-6906.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200311
ENTRY DATE: Entered STN: 2 Apr 2003
Last Updated on STN: 17 Dec 2003
Entered Medline: 28 Nov 2003

AB Advances in our understanding of fundamental biological processes can be made by the analysis of defects manifested in inherited diseases . The genes responsible for these genetic syndromes often encode proteins that act at critical points of the pathways that control biological processes such as cell proliferation, cell-cell communication, cellular differentiation, and cell death. This approach has lead to the discovery of novel gene products and/or biochemical pathways involved in disease, genes that in turn play a fundamental role in normal biological processes. This forward genetic approach, focusing on Mendelian disorders of vascular anomalies, has been particularly fruitful for the study of genetic regulation of angiogenesis. This review summarizes the ongoing saga of two genetic syndromes involving disruption of normal vascular morphogenesis. Each inherited disorder involves the focal development of a distinct vascular anomaly. In hereditary hemorrhagic telangiectasia (HHT), the hallmark vascular lesion is termed an arteriovenous malformation, which involves the direct communication of an artery with a vein (arteriovenous shunt), without an intervening capillary bed. For cerebral cavernous malformations (CCM), the lesions are grossly-dilated, closely-packed, capillary-like sinusoidal chambers. The autosomal dominant mode of inheritance of each of these distinct syndromes suggested that the underlying genes might regulate critical aspects of vascular morphogenesis. Emerging but intriguing tales are being told by the genes (and their protein products) mutated in these disorders.

L5 ANSWER 54 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003151545 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12667943
TITLE: Hereditary hemorrhagic telangiectasia: an update on transforming growth factor beta signaling in vasculogenesis and angiogenesis.
AUTHOR: van den Driesche Sander; Mummery Christine L; Westermann Cornelius J J
CORPORATE SOURCE: Hubrecht Laboratory, Netherlands Institute for Developmental Biology, Utrecht, The Netherlands.
SOURCE: Cardiovascular research, (2003 Apr 1) Vol. 58, No. 1, pp. 20-31. Ref: 79
Journal code: 0077427. ISSN: 0008-6363.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 2 Apr 2003
Last Updated on STN: 8 Jun 2003
Entered Medline: 6 Jun 2003

AB Hereditary hemorrhagic telangiectasia (HHT) is a vascular disorder in humans which has been mapped to two genes, endoglin and activin receptor-like kinase-1 (ALK-1) both of which mediate signaling by transforming growth factor beta ligands in vascular endothelial cells. Animal models have shown that these receptors are not only important for maintaining vascular integrity but also for angiogenesis both during embryonic development and during tumor growth. Here, we review the current status of reported mutations in the context of the clinical manifestations and the effects on the vessel wall both in patients and in animal models of the disease.

L5 ANSWER 55 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003129066 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12643470
TITLE: TGF-beta1/Smad signaling in prostate cancer.
AUTHOR: Bello-DeOcampo Diana; Tindall Donald J
CORPORATE SOURCE: Department of Biochemistry, Mayo Comprehensive Cancer Center, Rochester, Minnesota 55905, USA.
CONTRACT NUMBER: CA91956 (NCI)
DK60920 (NIDDK)
SOURCE: Current drug targets, (2003 Apr) Vol. 4, No. 3, pp. 197-207. Ref: 158
Journal code: 100960531. ISSN: 1389-4501.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 20 Mar 2003
Last Updated on STN: 22 May 2003
Entered Medline: 21 May 2003

AB Adenocarcinoma of the prostate is the most common type of cancer, excluding skin cancer, and the second leading cause of cancer death in adult men in the United States. The lifetime risk for developing symptomatic prostate cancer is one in five for an American man. A pivotal step in carcinogenesis is a shift in the balance between proliferation, differentiation, and apoptosis that favors cell proliferation. Transforming growth factor-beta (TGF -beta) is a key negative growth regulator in the normal prostate. Although TGF-beta) inhibits the proliferation of normal prostate cells and functions as a tumor suppressor in early tumorigenesis, it acts as a tumor promoter in later stages of tumor progression. Elevated expression of TGF-beta in prostate cancer cells is associated with poor clinical outcome. Over-expression of TGF -beta aids tumorigenesis by not only stimulating angiogenesis and suppressing the immune system, but also by acting directly on the prostate tumor cells. While prostate cancer cells become resistant to TGF -beta-induced growth inhibition and apoptosis, they retain other TGF-beta-induced responses that enhance tumorgenicity. such as induction of extracellular matrix proteins, cell adhesion proteins and proteases. These direct tumor effects are mediated primarily through Smad signaling. This review addresses the mechanisms by which prostate cancer cells may acquire TGF-beta resistance and promote tumorgenicity. Understanding the mechanisms underlying TGF-beta resistance is important for the identification and development of better diagnostic markers and more effective strategies for treating prostate cancer.

L5 ANSWER 56 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003124170 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12629334
TITLE: Peyronie's disease: a review.
AUTHOR: Gholami Shahram S; Gonzalez-Cadavid Nestor F; Lin Ching-Shwu; Rajfer Jacob; Lue Tom F
CORPORATE SOURCE: Knupps Molecular Urology Laboratory, Department of Urology, School of Medicine, University of California, San Francisco, 94143, USA.
CONTRACT NUMBER: G12RR-03026 (NCRR)
R01DK-53069 (NIDDK)
SOURCE: The Journal of urology, (2003 Apr) Vol. 169, No. 4, pp. 1234-41. Ref: 73
Journal code: 0376374. ISSN: 0022-5347.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 18 Mar 2003
Last Updated on STN: 3 Apr 2003
Entered Medline: 2 Apr 2003

AB PURPOSE: We provide a current review of Peyronie's disease. MATERIALS AND METHODS: We reviewed the world peer reviewed literature on the pathology, pathogenesis, diagnosis and treatment of Peyronie's disease. RESULTS: The incidence of Peyronie's disease has continuously increased during the last 30 years. However, fewer patients need prosthesis surgery as the sole treatment option because of earlier diagnosis, improved medical therapy, refinement in surgical technique and better understanding of the basic sciences of the disease. CONCLUSIONS: Currently patients with Peyronie's disease have had improvements in prognosis and experienced an expansion of the available therapeutic options.

L5 ANSWER 57 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003102048 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12615888
TITLE: IL-13 effector functions.
AUTHOR: Wynn Thomas A
CORPORATE SOURCE: Immunopathogenesis Section, Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892, USA.. twynn@niaid.nih.gov
SOURCE: Annual review of immunology, (2003) Vol. 21, pp. 425-56. Electronic Publication: 2001-12-19. Ref: 189
Journal code: 8309206. ISSN: 0732-0582.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 5 Mar 2003
Last Updated on STN: 28 Aug 2003
Entered Medline: 27 Aug 2003

AB IL-13 was first recognized for its effects on B cells and monocytes, where it upregulated class II expression, promoted IgE class switching and inhibited inflammatory cytokine production. It was also thought to be functionally redundant with IL-4. However, studies conducted with knockout mice, neutralizing antibodies, and novel antagonists demonstrate that IL-13 possesses several unique effector functions that distinguish it from IL-4. Resistance to most gastrointestinal nematodes is mediated by type-2 cytokine responses, in which IL-13 plays a dominant role. By regulating cell-mediated immunity, IL-13 modulates resistance to intracellular organisms including Leishmania major, Leishmania mexicana, and Listeria monocytogenes. In the lung, IL-13 is the central mediator of allergic asthma, where it regulates eosinophilic inflammation, mucus secretion, and airway hyperresponsiveness. Manipulation of IL-13 effector function may also prove useful in the treatment of some cancers like B-cell chronic lymphocytic leukemia and Hodgkin's disease, where IL-13 modulates apoptosis or tumor cell growth. IL-13 can also inhibit tumor immunosurveillance. As such, inhibitors of IL-13 might be effective as cancer immunotherapeutics by boosting type-1-associated anti-tumor defenses. Finally, IL-13 was revealed as a potent mediator of tissue fibrosis in both schistosomiasis and asthma, which indicates that it is a key regulator of the extracellular matrix. The mechanisms that regulate IL-13 production and/or function have also been investigated, and IL-4, IL-12, IL-18, IFN-gamma, IL-10, TGF-beta, TNF-alpha, and the IL-4/IL-13 receptor complex play important roles. This review highlights the effector functions of IL-13 and describes multiple pathways for modulating its activity in vivo.

L5 ANSWER 58 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003096207 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12608674
TITLE: Is platelet-rich plasma the perfect enhancement factor? A current review.
AUTHOR: Sanchez Andres R; Sheridan Phillip J; Kupp Leo I
CORPORATE SOURCE: Section of Periodontics, Department of Dental Specialties, Mayo Clinic, Rochester, Minnesota 55905, USA.. sanchez.andres@mayo.edu
SOURCE: The International journal of oral & maxillofacial implants, (2003 Jan-Feb) Vol. 18, No. 1, pp. 93-103.
Journal code: 8611905. ISSN: 0882-2786.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(META-ANALYSIS)
LANGUAGE: English
FILE SEGMENT: Dental Journals; Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 2 Mar 2003
Last Updated on STN: 11 Jun 2003
Entered Medline: 10 Jun 2003

AB Guided bone regeneration is an accepted surgical method employed in implant dentistry to increase the quantity and quality of the host bone in areas of localized alveolar defects. The lack of predictability in osseous regenerative procedures with various grafting materials suggests that improvement in the osteoinductive properties of these materials is highly desirable. Platelet-rich plasma (PRP), a modification of fibrin glue made from autologous blood, is being used to deliver growth factors in high concentration to sites requiring osseous grafting. Growth factors released from the platelets include platelet-derived growth factor, transforming growth factor beta, platelet-derived epidermal growth factor, platelet-derived angiogenesis factor, insulin-like growth factor 1, and platelet factor 4. These factors signal the local mesenchymal and epithelial cells to migrate, divide, and increase collagen and matrix synthesis. PRP has been suggested for use to increase the rate of bone deposition and quality of bone regeneration when augmenting sites prior to or in conjunction with dental implant placement Only 6 human studies using PRP have been found in the dental implant literature and 5 were case series or reports. Thus, there is clearly a lack of scientific evidence to support the use of PRP in combination with bone grafts during augmentation procedures. This novel and potentially promising technique requires well-designed, controlled studies to provide evidence of efficacy.

L5 ANSWER 59 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003094789 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12605568
TITLE: Treatment of scleroderma: an update.
AUTHOR: Sule Sangeeta D; Wigley Fredrick M
CORPORATE SOURCE: Division of Rheumatology, Johns Hopkins University, Baltimore, MD 21205, USA.
SOURCE: Expert opinion on investigational drugs, (2003 Mar) Vol. 12, No. 3, pp. 471-82. Ref: 63
Journal code: 9434197. ISSN: 1354-3784.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 28 Feb 2003
Last Updated on STN: 26 Aug 2003
Entered Medline: 25 Aug 2003

AB The goal of this article is to update the reader and focus on novel therapies and clinical trials published since our last

review [6]. Evidence suggests that drug intervention should target one or all of three biological processes: vascular disease, autoimmunity and tissue fibrosis. Efforts should be made to classify the subtype of scleroderma, to determine the activity of the disease process and the degree of specific organ involvement before specific treatment decisions are made. Cyclophosphamide in fibrosing alveolitis, intravenous prostaglandins and other vasodilators for the vascular disease, endothelin-1 inhibition in pulmonary hypertension and immunosuppressive therapy for early inflammatory disease, all appear to have benefit. Several agents used in vitro and in animal models of fibrosis also show promise including anti-transforming growth factor-beta, the statins and anti-integrins. More experience in well-designed clinical trials is needed to define the role of these agents in treating scleroderma.

L5 ANSWER 60 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003077359 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12542972
TITLE: Genetic polymorphisms and cancer susceptibility of breast cancer in Korean women.
AUTHOR: Kang Daehee
CORPORATE SOURCE: Department of Preventive Medicine, Seoul National University College of Medicine, Seoul 110-799, Korea.. dhkang@snu.ac.kr
SOURCE: Journal of biochemistry and molecular biology, (2003 Jan 31) Vol. 36, No. 1, pp. 28-34. Ref: 12
Journal code: 9702084. ISSN: 1225-8687.
PUB. COUNTRY: Korea (South)
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 21 Feb 2003
Last Updated on STN: 21 Jun 2003
Entered Medline: 20 Jun 2003
AB Breast cancer is the most prevalent cancer among women in Western countries, and its prevalence is also increasing in Asia. The major risk factor for breast cancer can be traced to reproductive events that influence the lifetime levels of hormones. However, a large percentage of breast cancer cases cannot, be explained by these risk factors. The identification of susceptibility factors that predispose individuals to breast cancer (for instance, if they are exposed to particular environmental agents) could possibly give further insight into the etiology of this malignancy and provide targets for the future development of therapeutics. The most interesting candidate genes include those that mediate a range of functions. These include carcinogen metabolism, DNA repair, steroid hormone metabolism, signal transduction, and cell cycle control. we conducted a hospital-based case-control study on South Korea to evaluate the potential modifying role of the genetic pollymprphisms of selected low penetrance gens that are involved carcinogen metabolisms (i.e., CYP1A1, CYP2E1, GSTM1/T1/P1, NAT1/2, etc.), estrogen synthesis and metabolism (i.e., CYP19, CYP17, CYP1B1, COMT, ER-alpha, etc.), DNA repair (i.e., XRCC1/3, ERCC2/4, ATM, AGT, etc.), and signal transduction as well as others (i.e., TGF- beta, IGF-1, TNF- beta, IL-1B, IL-1RN, etc.). We also took into account the potential interaction between these and the known risk factors of breast cancer. The results of selected genes will be presented in this mini-review.

L5 ANSWER 61 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003071265 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12582309
TITLE: Role of intestinal flora in the development of allergy.
AUTHOR: Kalliomaki Marko; Isolauri Erika
CORPORATE SOURCE: Department of Pediatrics, University of Turku, Finland.. marko.kalliomaki@utu.fi
SOURCE: Current opinion in allergy and clinical immunology, (2003 Feb) Vol. 3, No. 1, pp. 15-20. Ref: 69
Journal code: 100936359. ISSN: 1528-4050.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 14 Feb 2003
Last Updated on STN: 12 Jun 2003
Entered Medline: 11 Jun 2003
AB PURPOSE OF REVIEW: The frequency of allergic diseases is increasing worldwide. Experimental and clinical studies have linked a reduced number of early infections to this trend. The gastrointestinal system, which comprises the largest lymphoid tissue and microbial reservoir of the body, has received more attention during the last few years as a potential determiner in the development of atopic disease. RECENT FINDINGS: Alterations in intestinal microbiota have been detected both in infants suffering from allergic disease and in those later developing the disorder. Delay in the compositional development of and in gut microflora was a general finding in allergic children. In a subsequent study, perinatal administration of lactobacilli halved the later development of atopic eczema during the first 2 years of life. Specific strains of the healthy gut microbiota have been shown to induce the production of IL-10 and transforming growth factor-beta, which possess an important regulative role in the development of allergic type immune response. Probiotics also strengthen gut defence barrier mechanisms and reduce antigen load in the gut. Pattern recognition receptors in intestinal epithelial and antigen-presenting cells have been demonstrated to mediate a continuing dialogue between host and gut microbiota. SUMMARY: Despite several promising findings, the exact role of gut normal microbiota in the development of allergy remains to be elucidated. For successful interventions, more data concerning a communication between host and specific microbial species are needed.

L5 ANSWER 62 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003069134 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12579464
TITLE: [The role of cytokines and growth factors in fibroproliferative lung disease].
Die Bedeutung von Zytokinen und Wachstumsfaktoren bei fibrosierenden Lungenerkrankungen.
AUTHOR: Kolb M; Schmidt M
CORPORATE SOURCE: Medizinische Klinik der Julius-Maximilian-Universitat Wurzburg, Schwerpunkt Pneumologie.. kolb_m@klinik.uni-wuerzburg.de
SOURCE: Pneumologie (Stuttgart, Germany), (2003 Feb) Vol. 57, No. 2, pp. 91-7. Ref: 74
Journal code: 8906641. ISSN: 0934-8387.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 12 Feb 2003
Last Updated on STN: 18 Apr 2003
Entered Medline: 17 Apr 2003
AB A new hypothesis of the pathogenesis of fibroproliferative lung disease suggests that fibrosis is caused by abnormal and excessive wound healing and pathologic tissue remodelling. Inflammation is possibly an

epiphenomenon. Cytokines are critical players in the pathologic process and attractive targets for pharmacological intervention. TGF beta is a key profibrotic growth factor, a variety of approaches are known to modify and inhibit its activity. This article reviews the basic pathological concepts of pulmonary fibrogenesis and outlines its potential clinical benefit.

L5 ANSWER 63 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003069104 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12579392
TITLE: Diabetic nephropathy: renal development gone awry?.
AUTHOR: Dolan Vincent; Hensey Carmel; Brady Hugh R
CORPORATE SOURCE: Department of Medicine and Therapeutics, Conway Institute of Biomolecular and Biomedical Research, University College Dublin, The Mater Misericordiae Hospital, Dublin, Ireland.
SOURCE: Pediatric nephrology (Berlin, Germany), (2003 Feb) Vol. 18, No. 2, pp. 75-84. Electronic Publication: 2002-11-22. Ref: 69
Journal code: 8708728. ISSN: 0931-041X.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 12 Feb 2003
Last Updated on STN: 17 Sep 2003
Entered Medline: 16 Sep 2003
AB Nephrogenesis is controlled by a sequence of inductive signals between different areas of the developing kidney. As these signals are being elucidated, it has become clear that many important developmental genes are re-expressed in the mature organ following injury, possibly as part of repair and regeneration. While this reuse of developmental pathways may contribute to healing and repair, it may alternatively result in scar formation if specific components of the pathways are missing, if the temporal correlation of various elements is faulty, or if an injurious stimulus persists. In the review we will use diabetic nephropathy as an example to illustrate this paradigm in renal disease. The pathogenesis of diabetic nephropathy is complex and characterized by altered expression of many genes, including growth factors, apoptotic regulators, cellular matrix components, and cytoskeletal proteins. Many of these factors also function during kidney development. The elucidation of the roles these genes play in nephrogenesis and of their array of molecular partners and modulators may ultimately shed light on the pathogenesis of disease (and indeed vice versa), and may even suggest new therapeutic strategies.

L5 ANSWER 64 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003061194. MEDLINE
DOCUMENT NUMBER: PubMed ID: 12570836
TITLE: New aspects of cyclosporin a mode of action: from gene silencing to gene up-regulation.
AUTHOR: Mascarell Laurent; Truffa-Bachi Paolo
CORPORATE SOURCE: Unite Biologie des Populations Lymphocytaires, CNRS URA 1961, Institut Pasteur, Paris, France.
SOURCE: Mini reviews in medicinal chemistry, (2003 May) Vol. 3, No. 3, pp. 205-14. Ref: 80
Journal code: 101094212. ISSN: 1389-5575.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 7 Feb 2003
Last Updated on STN: 14 May 2003
Entered Medline: 13 May 2003
AB Cyclosporin A (CSA) has transformed clinical transplantation, both in term of success and of quality-of-life of the patient. Studies aimed to unfold the site of CSA action have shown that this molecule binds to cytosolic proteins of the cyclophilin family. CSA:cyclophilin complexes have a high affinity for calcineurin, a key enzyme in T-cell activation. By blocking the calcineurin activity, CSA prevents the induction of genes encoding for cytokines and their receptors. Thus, humoral and cellular immune responses are abolished, this resulting in the successful graft acceptance. Disappointingly, CSA and the other molecules as FK506, sharing the capacity to inhibit calcineurin, should be administered for all patient life, as tolerance to alloantigens is not achieved by these molecules. The long term utilization of this class of immunosuppressors increases the incidence of different tumors. The finding that CSA does not interfere with various biochemical pathways has prompted different groups to analyze a possible effect of CSA on molecules that might be involved in different functions of the immune response and/or in tumorogenesis. A new picture of CSA mode of action is emerging in which the immunosuppressor prevents the transcription of a group of genes, concomitantly inducing the transcription of another set. Here, we review the data and discuss the consequences of these new findings in term of T-cell activation mechanisms.

L5 ANSWER 65 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003050437 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12561070
TITLE: Heterotopic ossification in rectal cancer: Rare finding with a novel proposed mechanism.
AUTHOR: Kypson Alan P; Morphew Emilie; Jones Relief; Gottfried Marcia R; Seigler Hilliard F
CORPORATE SOURCE: Department of Surgery, Duke University Medical Center, Durham, North Carolina 27710, USA.
SOURCE: Journal of surgical oncology, (2003 Feb) Vol. 82, No. 2, pp. 132-6; disccussion 137. Ref: 33
Journal code: 0222643. ISSN: 0022-4790.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 2 Feb 2003
Last Updated on STN: 19 Mar 2003
Entered Medline: 18 Mar 2003
AB The rare finding of heterotopic ossification in a case of primary rectal adenocarcinoma is described along with a review of the literature. Immunohistochemistry for a bone morphogenic protein (BMP-2) and fibroblast growth factor (FGF-2), both of which induce and stimulate bone formation, was performed and revealed overexpression of BMP-2 by the tumor cells, elucidating a possible mechanism which up to now had been based merely on speculation.

L5 ANSWER 66 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003048387 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12558073
TITLE: Cytokine polymorphisms in chronic inflammatory diseases with reference to occupational diseases.
AUTHOR: Yucesoy Berran; Kashon Michael L; Luster Michael I
CORPORATE SOURCE: Ankara University, Faculty of Pharmacy, Department of Toxicology, 06100, Tandogan-Ankara, Turkey..
BYucesoy@cdc.gov

SOURCE: Current molecular medicine, (2003 Feb) Vol. 3, No. 1, pp. 39-48. Ref: 141
Journal code: 101093076. ISSN: 1566-5240.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 2 Feb 2003
Last Updated on STN: 16 Jul 2003
Entered Medline: 15 Jul 2003

AB Genes which encode inflammatory cytokines are subject to polymorphisms in their regulatory regions that may effect both the level and ratio of cytokines produced in response to exogenous stimuli. These variant alleles are observed in a large percent of the population and are often associated with increased or decreased susceptibility or severity (modifiers) to infectious, immune or inflammatory diseases. Environmental factors can also play either a direct (i.e., causative factor) or indirect (modifying factor) role in these diseases. Thus, it would follow that gene-environment interactions would effect the expression and/or progression of the disease. In the present review, the concept that some of the common allelic variants found in cytokine genes represent modifying factors in chronic inflammatory diseases associated with occupational exposure is discussed.

L5 ANSWER 67 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003047099 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12556204
TITLE: The not-so innocent bystander: the microenvironment as a therapeutic target in cancer.
AUTHOR: Erickson Anna C; Barcellos-Hoff Mary Helen
CORPORATE SOURCE: Life Sciences Division, Building 74-174, 1 Cyclotron Road, Lawrence Berkeley National Laboratory, Berkeley, CA 94720, USA.
SOURCE: Expert opinion on therapeutic targets, (2003 Feb) Vol. 7, No. 1, pp. 71-88. Ref: 184
Journal code: 101127833. E-ISSN: 1744-7631.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200605
ENTRY DATE: Entered STN: 31 Jan 2003
Last Updated on STN: 17 Dec 2003
Entered Medline: 1 May 2006

AB The microenvironment in which cancer arises is often regarded as a bystander to the clonal expansion and acquisition of malignant characteristics of the tumour. However, a major function of the microenvironment is to suppress cancer, and its disruption is required for the establishment of cancer. In addition, tumour cells can further distort the microenvironment to promote growth, recruit non-malignant cells that provide physiological resources, and facilitate invasion. In this review, the authors discuss the contribution of the microenvironment, i.e., the stroma and its resident vasculature, inflammatory cells, growth factors and the extracellular matrix (ECM), in the development of cancer, and focus on two components as potential therapeutic targets in breast cancer. First, the ECM, which imparts crucial signalling via integrins and other receptors, is a first-line barrier to invasion, modulates aggressive behaviour and may be manipulated to provide novel impediments to tumour growth. Second, the authors discuss the involvement of TGF-beta1 as an example of one of many growth factors that can regulate ECM composition and degradation and that play complex roles in cancer. Compared to the variable routes taken by cells to become cancers, the response of tissues to cancer is relatively consistent. Therefore, controlling and eliminating cancer may be more readily achieved indirectly via the tissue microenvironment.

L5 ANSWER 68 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003044846 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12555288
TITLE: Growth factors in the treatment of diabetic foot ulcers.
AUTHOR: Bennett S P; Griffiths G D; Schor A M; Leese G P; Schor S L
CORPORATE SOURCE: Unit of Cell and Molecular Biology, The Dental School, University of Dundee, Dundee, UK.. s.p.bennett@doctors.org.uk
SOURCE: The British journal of surgery, (2003 Feb) Vol. 90, No. 2, pp. 133-46. Ref: 130
Journal code: 0372553. ISSN: 0007-1323.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 30 Jan 2003
Last Updated on STN: 26 Mar 2003
Entered Medline: 25 Mar 2003

AB BACKGROUND: Chronic foot ulceration is a major source of morbidity in diabetic patients. Despite traditional comprehensive wound management, including vascular reconstruction, there remains a cohort of patients with non-responding wounds, often resulting in amputation. These wounds may benefit from molecular manipulation of growth factors to enhance the microcirculation. METHODS: A review of the current literature was performed using Pubmed, with secondary references obtained from key articles. RESULTS AND CONCLUSION: There has been a generally disappointing clinical outcome from growth factor trials, although topical platelet-derived growth factor has shown significant benefit and should be considered in non-healing, well perfused ulcers after failure of conventional wound care. The modulatory role of the extracellular matrix in the cellular response to growth factors and data from regenerative-type fetal wound healing are further areas of interest. The chemical induction of microvessel formation may become a future therapeutic option.

L5 ANSWER 69 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003039398 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12546640
TITLE: Role of transforming growth factor beta in conjunctival scarring.
AUTHOR: Cordeiro M Francesca
CORPORATE SOURCE: Department of Pathology, Moorfields Eye Hospital and Institute of Ophthalmology, Bath Street, London EC1V 9EL, UK.. m.cordeiro@ucl.ac.uk
SOURCE: Clinical science (London, England : 1979), (2003 Feb) Vol. 104, No. 2, pp. 181-7. Ref: 49
Journal code: 7905731. ISSN: 0143-5221.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 28 Jan 2003
Last Updated on STN: 1 Apr 2003
Entered Medline: 31 Mar 2003

AB Glaucoma is the major cause of irreversible blindness throughout the

world. Of all of the treatments that are available at present, the most effective appears to be surgery; however, excessive conjunctival scarring can lead to surgical failure. In the last decade, the introduction of the anti-metabolites mitomycin-C and 5-fluorouracil as anti-scarring treatments have greatly improved the results of glaucoma surgery, but these agents are associated with complications that can potentially result in blindness. A possible target for a more physiological approach to anti-scarring is transforming growth factor beta. This review examines the role of transforming growth factor beta in conjunctival scarring and discusses promising new ways of modifying its activity.

L5 ANSWER 70 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003033502 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12540741
TITLE: Novel pharmacological approaches to manage interstitial lung fibrosis in the twenty-first century.
AUTHOR: Giri Shri N
CORPORATE SOURCE: Department of Molecular Biosciences, School of Veterinary Medicine, University of California, Davis, California 95616, USA.. sngiri@ucdavis.edu
SOURCE: Annual review of pharmacology and toxicology, (2003) Vol. 43, pp. 73-95. Electronic Publication: 2002-01-10. Ref: 163
Journal code: 7607088. ISSN: 0362-1642.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 24 Jan 2003
Last Updated on STN: 10 Sep 2003
Entered Medline: 9 Sep 2003
AB Pharmacological agents currently in use to treat interstitial lung fibrosis are either ineffective or too toxic in humans. This review addresses mechanistically based novel approaches that have the potential to minimize the accumulation of collagen in the lung, a hallmark of lung fibrosis. These approaches include maintaining the intracellular levels of NAD(+) and ATP, blocking the biological activities of TGF-beta and integrins, evaluating the effectiveness of PAF-receptor antagonists and NOS inhibitors, and developing a new generation of cysteine pro-drugs with an adequate degree of bioavailability. A critical analysis of each approach as it relates to management of IPF in humans is presented.

L5 ANSWER 71 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003031591 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12539179
TITLE: Angiogenesis in normal and neoplastic pituitary tissues.
AUTHOR: Lloyd Ricardo V; Vidal Sergio; Horvath Eva; Kovacs Kalman; Scheithauer Bernd
CORPORATE SOURCE: Department of Laboratory Medicine, Mayo Clinic, Rochester, Minnesota 55905, USA.
CONTRACT NUMBER: CA90249 (NCI)
SOURCE: Microscopy research and technique, (2003 Feb 1) Vol. 60, No. 2, pp. 244-50. Ref: 91
Journal code: 9203012. ISSN: 1059-910X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 23 Jan 2003
Last Updated on STN: 18 Jul 2003
Entered Medline: 17 Jul 2003
AB Angiogenesis, or the formation of new blood vessels, is a dynamic process needed for embryogenesis, post-natal growth, morphogenesis, tumorigenesis, and for other biological processes. Angiogenesis is very important for tumor development and progression. This review examines the activators and inhibitors of angiogenesis with emphasis on the pituitary gland and pituitary neoplasms. Some of the proteins regulating angiogenesis in pituitary tumors such as vascular endothelial growth factor (VEGF) and VEGF receptors, fibroblasts growth factors (FGF), transforming growth factor beta (TGFB), interleukins, interferons, and matrix metalloproteinases (MMPs) and inhibitors of MMPs have been examined in animal and human pituitary tumor models. However, many other significant regulators of angiogenesis including angiopoietins, angiostatin, and thrombospondins have not been studied extensively in pituitary tumors to date. Newer concepts and developments in angiogenesis such as vasculogenic mimicry and gene therapy approaches to angiogenesis in cancer treatment are also discussed.

L5 ANSWER 72 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003030929 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12537941
TITLE: Antisense oligonucleotide therapy for urologic tumors.
AUTHOR: Kausch Ingo; Bohle Andreas
CORPORATE SOURCE: Department of Urology, Medical University of Lubeck, Ratzeburger Allee 160, Germany.
SOURCE: Current urology reports, (2003 Feb) Vol. 4, No. 1, pp. 60-9. Ref: 83
Journal code: 100900943. ISSN: 1527-2737.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 23 Jan 2003
Last Updated on STN: 3 Apr 2003
Entered Medline: 2 Apr 2003
AB Modulation of gene expression using antisense oligonucleotides has advanced from the laboratory to the clinic. Numerous companies can, at least partially, attribute their success to the development of antisense techniques, and one antisense drug is currently on the market. Antisense compounds have been used in clinical trials that included patients with urologic tumors, mostly directed at proliferation- or apoptosis-related targets. Furthermore, therapeutic inhibition of many new identified genes is being investigated in preclinical tests. This review provides a contemporary overview of current preclinical and clinical antisense oligonucleotide concepts for the treatment of urologic tumors.

L5 ANSWER 73 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2003030845 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12538447
TITLE: Prevention of ovarian cancer: intraepithelial neoplasia.
AUTHOR: Brewer Molly A; Johnson Karen; Follen Michele; Gershenson David; Bast Robert Jr
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Arizona Cancer Center, University of Arizona, Tucson, Arizona 85724, USA.. mbrewer@azcc.arizona.edu
SOURCE: Clinical cancer research : an official journal of the American Association for Cancer Research, (2003 Jan) Vol. 9, No. 1, pp. 20-30. Ref: 107

Journal code: 9502500. ISSN: 1078-0432.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 23 Jan 2003
Last Updated on STN: 18 Jul 2003
Entered Medline: 17 Jul 2003

AB To reduce the incidence and mortality associated with invasive cancers, the Intraepithelial Neoplasia (IEN) Task Force recommends that carcinogenesis be viewed as a disease that requires treatment. This publication outlines the current knowledge of IEN of the ovary and reviews chemoprevention possibilities for ovarian cancer. Ovarian cancer has the highest mortality of all of the gynecological cancers and is the fourth leading cause of death from cancer in women. The IEN Task Force has defined precancer as a noninvasive lesion that has genetic abnormalities, loss of cellular control functions, and some phenotypic characteristics of invasive cancer with a substantial likelihood of developing invasive cancer. The IEN Task Force recommends targeting moderate to severe dysplasia for new IEN treatment agents in clinical trials. Ovarian cancer does not have a clear preinvasive lesion yet merits considerable study for new prevention strategies because of the high mortality associated with ovarian cancer. There is a great unmet clinical need for treatments that can prevent ovarian cancer by providing nonsurgical options that treat the entire epithelial layer. New prevention strategies hold significant promise to reduce the mortality from ovarian cancer.

L5 ANSWER 74 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2002733379 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12496662
TITLE: Tubular epithelial-myofibroblast transdifferentiation mechanisms in proximal tubule cells.
AUTHOR: Lan Hui Y
CORPORATE SOURCE: Department of Medicine-Nephrology, Baylor College of Medicine, Houston, Texas 77030, USA.. hlan@bcm.tmc.edu
SOURCE: Current opinion in nephrology and hypertension, (2003 Jan) Vol. 12, No. 1, pp. 25-9. Ref: 33
Journal code: 9303753. ISSN: 1062-4821.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 27 Dec 2002
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Entered Medline: 9 Jul 2003

AB PURPOSE OF REVIEW: Emerging evidence suggests that tubular epithelial-myofibroblast transdifferentiation is an important event in renal tubulointerstitial fibrosis. This review describes the recent findings in the context of the tubular epithelial-myofibroblast transdifferentiation process and discusses the possible mechanisms involved. RECENT FINDINGS: Tubular epithelial-myofibroblast transdifferentiation is a complex process involving disruption of polarized tubular epithelial cell morphology into cells with spindle-shaped mesenchymal morphology, formation of actin stress fibers, loss of cell-cell adhesions through downregulation of E-cadherin, destruction of basement membrane, and increased cell migration and invasion. This phenotypic transition has also been recently reported in human glomerulonephritis with progressive tubulointerstitial fibrosis. Transforming growth factor-beta is a key fibrogenic growth factor that regulates tubular epithelial-myofibroblast transdifferentiation, which is counter-regulated by hepatocyte growth factor. In addition, basic fibroblast growth factor, advanced glycation end products, and angiotensin II have also been reported to induce the process. Importantly, the recent discovery of transforming growth factor-beta/Smad signaling has allowed the delineation of the intracellular mechanisms of tubular epithelial-myofibroblast transdifferentiation. Indeed, Smad signaling is a key pathway whereby transforming growth factor-beta and angiotensin II induce tubular epithelial-myofibroblast transdifferentiation in vitro. This involves the activation of transforming growth factor-beta receptor-associated Smad2 and is inhibited by an inhibitory Smad protein, Smad7. Thus, Smad signaling plays a critical role in tubular epithelial-myofibroblast transdifferentiation. SUMMARY: Renal myofibroblasts may be derived from tubular epithelial cells by a process of tubular epithelial-myofibroblast transdifferentiation. Transforming growth factor-beta signals through Smads to positively or negatively regulate this process. Blockade of this process by either hepatocyte growth factor or targeting the Smad signaling pathway may provide novel therapeutic strategies to combat renal fibrosis.

L5 ANSWER 75 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2002722583 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12486316
TITLE: Substance p-fibronectin-cytokine interactions in myeloproliferative disorders with bone marrow fibrosis.
AUTHOR: Rameshwar P; Oh H S; Yook C; Gascon P; Chang V T
CORPORATE SOURCE: Department of Medicine, UMDNJ New Jersey Medical School, Newark, N.J. 07103, USA.. rameshwa@umdnj.edu
CONTRACT NUMBER: CA-89868 (NCI)
HL-54973 (NHLBI)
HL-57675 (NHLBI)
SOURCE: Acta haematologica, (2003) Vol. 109, No. 1, pp. 1-10. Ref: 74
Journal code: 0141053. ISSN: 0001-5792.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
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LANGUAGE: English
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ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 18 Dec 2002
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AB Bone marrow (BM) fibrosis could occur secondarily to several clinical disorders: hematological and nonhematological. Clinical presentation of fibrosis could occur in myeloproliferative diseases, lymphoma, myelodysplastic syndrome and myeloma. The pathophysiology underlying BM fibrosis remains unclear despite intensive study, with a corresponding lack of specific therapy. This review discusses new insights in the role of substance P, cytokines and fibronectin in the development of BM fibrosis. Substance P is a neuropeptide that possesses pleiotropic properties, e.g. neurotransmission and immune/hematopoietic modulation and is linked to BM fibrosis. Cytokines and growth factors, in particular those associated with fibrogenic properties, e.g. TGF-beta, IL-1 and platelet-derived growth factor, are linked to BM fibrosis. Extracellular matrix proteins are increased in patients with BM fibrosis. Fibronectin in the sera of patients with BM fibrosis is complexed to substance P. Fibronectin appears to protect substance P from degradation by endogenous peptidases. This review describes the preliminary findings on the colocalization of substance P and fibronectin in the BM of patients with fibrosis. These data are reviewed in the context of published reports with particular focus on the relevant cytokines. A more detailed

understanding of intra- and intercellular mechanisms in BM fibrosis may lead to effective therapy.

L5 ANSWER 76 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2002715447 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12477368
TITLE: Can thermal lasers promote skin wound healing?.
AUTHOR: Capon Alexandre; Mordon Serge
CORPORATE SOURCE: Lille University Hospital, Lille, France.
SOURCE: American journal of clinical dermatology, (2003) Vol. 4, No. 1, pp. 1-12. Ref: 149
Journal code: 100895290. ISSN: 1175-0561.
PUB. COUNTRY: New Zealand
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
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ENTRY DATE: Entered STN: 17 Dec 2002
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Entered Medline: 15 Apr 2003

AB Lasers are now widely used for treating numerous cutaneous lesions, for scar revision (hypertrophic and keloid scars), for tissue welding, and for skin resurfacing and remodeling (wrinkle removal). In these procedures lasers are used to generate heat. The modulation of the effect (volatilization, coagulation, hyperthermia) of the laser is obtained by using different wavelengths and laser parameters. The heat source obtained by conversion of light into heat can be very superficial, yet intense, if the laser light is well absorbed (far-infrared:CO(2) or Erbium:Yttrium Aluminum Garnet [Er:YAG] lasers), or it can be much deeper and less intense if the laser light is less absorbed by the skin (visible or near-infrared). Lasers transfer energy, in the form of heat, to surrounding tissues and, regardless of the laser used, a 45-50 degrees C temperature gradient will be obtained in the surrounding skin. If a wound healing process exists, it is a result of live cells reacting to this low temperature increase. The generated supraphysiologic level of heat is able to induce a heat shock response (HSR), which can be defined as the temporary changes in cellular metabolism. These changes are rapid and transient, and are characterized by the production of a small family of proteins termed the heat shock proteins (HSP). Recent experimental studies have clearly demonstrated that HSP 70, which is over-expressed following laser irradiation, could play a role with a coordinated expression of other growth factors such as transforming growth factor (TGF)-beta. TGF-beta is known to be a key element in the inflammatory response and the fibrogenic process. In this process, the fibroblasts are the key cells since they produce collagen and extracellular matrix. In conclusion, the analysis of the literature, and the fundamental considerations concerning the healing process when using thermal lasers, are in favor of a modification of the growth factors synthesis after laser irradiation, induced by an HSR. An extensive review of the different techniques and several clinical studies confirm that thermal lasers could effectively promote skin wound healing, if they are used in a controlled manner.

L5 ANSWER 77 OF 77 MEDLINE on STN
ACCESSION NUMBER: 2002706420 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12469181
TITLE: Cellular signaling pathways affect the function of ribonucleotide reductase mRNA binding proteins: mRNA stabilization, drug resistance, and malignancy (Review).
AUTHOR: Burton Teralee R; Kashour Tarek; Wright Jim A; Amara Francis M
CORPORATE SOURCE: St. Boniface General Hospital Research Center, Winnipeg, MB, R2H 2A6, Canada.
SOURCE: International journal of oncology, (2003 Jan) Vol. 22, No. 1, pp. 21-31. Ref: 84
Journal code: 9306042. ISSN: 1019-6439.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 17 Dec 2002
Last Updated on STN: 17 Jun 2003
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AB Ribonucleotide reductase is an enzyme that is essential for DNA synthesis and repair. It is composed of 2 dimeric proteins called R1 and R2 that are both necessary for enzymatic activity that reduces ribonucleotides to deoxyribonucleotides. This is the rate-limiting reaction that provides a supply of precursors for DNA synthesis therefore it is essential for cell proliferation. The importance of understanding the complex regulation of ribonucleotide reductase is emphasized by observations that mechanisms controlling its expression and activity may be altered during malignant cell proliferation which leads to drug resistance, making it a useful target to develop chemotherapeutic compounds in the treatment of cancer. Expression studies with the R1 and R2 genes have provided evidence for a direct role for the components of ribonucleotide reductase in determining malignant potential. Ribonucleotide reductase is regulated by transcriptional activation of gene expression and post-transcriptional mechanisms that alter mRNA message stability. Post-transcriptional regulation of mRNA turnover plays an important role in modulating mRNA steady state levels and therefore directly influences gene expression. The 3'-untranslated region (UTR) of R1 and R2 messages contain sequences that are important in regulating gene expression through changes in message stability. Studies have found that mRNA message stability is mediated by growth factors, cytokines and tumor promoters. Several studies have elucidated signal transduction pathways of tumor promoters, TGF-beta and oxidation/reduction agents. This report reviews how knowledge of these signaling pathways is revealing new insights into how ribonucleotide reductase mRNA binding proteins are important in regulating cellular proliferation, drug resistance and malignancy.

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